```
=> fil capl; d que l13
FILE 'CAPLUS' ENTERED AT 14:59:04 ON 19 OCT 2006
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FILE COVERS 1907 - 19 Oct 2006  VOL 145 ISS 17
FILE LAST UPDATED: 18 Oct 2006  (20061018/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L13             1 SEA FILE=CAPLUS ABB=ON  US2004-501140/AP
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Inventor search

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=> d ibib ed abs l13

L13  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:492255  CAPLUS
DOCUMENT NUMBER:          141:52965
TITLE:                    Cephalexin biosynthesis by polymer immobilized
                          penicillin amidase
INVENTOR(S):              Menzler, Stefan; Boller, Thomas; Petereit,
                          Hans-Ulrich; Meier, Christian
PATENT ASSIGNEE(S):       Roehm GmbH & Co. KG, Germany
SOURCE:                   Ger. Offen., 9 pp.
                          CODEN: GWXXBX
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.            KIND   DATE        APPLICATION NO.         DATE
     ---------------       ----   --------    --------------------    --------
     DE 10256656            A1    20040617    DE 2002-10256656        20021203
     WO 2004050893          A1    20040617    WO 2003-EP11480         20031016
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR,
             TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
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BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003283271 A1 20040623 AU 2003-283271 20031016
EP 1466006 A1 20041013 EP 2003-775191 20031016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2005084925 A1 20050421 US 2004-501140 20031016 <--
CN 1685059 A 20051019 CN 2003-80100024 20031016
JP 2006500957 T2 20060112 JP 2004-556086 20031016
PRIORITY APPLN. INFO.: DE 2002-10256656 A 20021203
WO 2003-EP11480 W 20031016

ED Entered STN: 18 Jun 2004

AB A process is provided for the enzymic biosynthesis of cephalexin by a penicillin amidase immobilized on a copolymer. The copolymer used is composed of methacrylamide, allyl glycidyl ether, glycidyl methacrylate and methylene-bis-methacrylamide. The immobilized biocatalyst then serves to catalyze the acylation of 7-aminodesacetoxycephalosporanic acid with D-phenylglycinamde.

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=> fil capl; d que l20; d que l30; s l20,l30 not l13
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FILE LAST UPDATED: 18 Oct 2006  (20061018/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L14 (     84829)SEA FILE=REGISTRY ABB=ON  191.74.3/RID
L15 (      7691)SEA FILE=CAPLUS ABB=ON  L14/P
L16 (        51)SEA FILE=REGISTRY ABB=ON  PENICILLIN AMIDASE?/CN
L17 (      1995)SEA FILE=CAPLUS ABB=ON  L16
L18 (   1525213)SEA FILE=CAPLUS ABB=ON  POLYMER?/OBI
L19 (    484949)SEA FILE=CAPLUS ABB=ON  RESIN#/OBI
L20           10 SEA FILE=CAPLUS ABB=ON  L15 AND L17 AND (L18 OR L19)
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= all compounds containing

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L22 (      7691)SEA FILE=CAPLUS ABB=ON  L21/P
L23 (        51)SEA FILE=REGISTRY ABB=ON  PENICILLIN AMIDASE?/CN
L24 (      1995)SEA FILE=CAPLUS ABB=ON  L23
L25 (       363)SEA FILE=CAPLUS ABB=ON  L24(L)CAT/RL
L26 (    416467)SEA FILE=CAPLUS ABB=ON  ?ACRYLAMID?/BI OR ?METHACRYL?/BI
L27 (         1)SEA FILE=REGISTRY ABB=ON  25014-41-9
L28 (         1)SEA FILE=REGISTRY ABB=ON  129825-50-9
L29 (     16503)SEA FILE=CAPLUS ABB=ON  (L27 OR L28)
L30           11 SEA FILE=CAPLUS ABB=ON  L25 AND L22 AND (L26 OR L29)

L36           15 (L20 OR L30) NOT L13
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printed with inventor search

```
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FILE 'CASREACT' ENTERED AT 14:59:52 ON 19 OCT 2006
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for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 15 Oct 2006 VOL 145 ISS 16

New CAS Information Use Policies, enter HELP USAGETERMS for details.

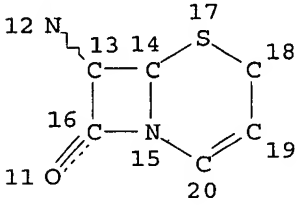
****
*
* CASREACT now has more than 10 million reactions *
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L4 STR

RRT



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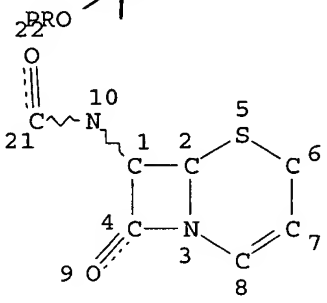

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L6 909 SEA FILE=CASREACT SSS FUL L4 (11379 REACTIONS)

100.0% DONE 11500 VERIFIED 11379 HIT RXNS 909 DOCS
SEARCH TIME: 00.00.02

L1 51 SEA FILE=REGISTRY ABB=ON PENICILLIN AMIDASE?/CN
L4 STR
L6 909 SEA FILE=CASREACT SSS FUL L4 (11379 REACTIONS)
L7 122 SEA FILE=CASREACT ABB=ON L1/CAT
L8 35 SEA FILE=CASREACT ABB=ON L6 AND L7
L9 26925 SEA FILE=CASREACT ABB=ON POLYMER? OR RESIN#
L11 4600 SEA FILE=CASREACT ABB=ON COAT? OR IMMOBILI?
L12 19 SEA FILE=CASREACT ABB=ON L8 AND (L9 OR L11)

Searched by Barb O'Bryen, STIC 2-2518

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=> dup rem l12,l36
FILE 'CASREACT' ENTERED AT 14:59:57 ON 19 OCT 2006
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PROCESSING COMPLETED FOR L12
PROCESSING COMPLETED FOR L36
L37          33 DUP REM L12 L36 (1 DUPLICATE REMOVED)
                ANSWERS '1-19' FROM FILE CASREACT
                ANSWERS '20-33' FROM FILE CAPLUS

=> d ibib abs hit 1-19; d ibib ed abs hitstr 20-33; fil hom


L37  ANSWER 1 OF 33  CASREACT  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         126:89175  CASREACT
TITLE:                    Penicillin amidase-catalyzed preparative synthesis of
                          cephem 7-(benzoxazolon-3-ylacetamido)desacetoxycephalo
                          sporanic acid using a non-specific
                          polyethyleneglycol-modified acyl donor
AUTHOR(S):                Mincheva, Z.; Stambolieva, N.; Petrova, K.; Galunsky,
                          B.
CORPORATE SOURCE:         Dep. Chemistry, Sofia Univ., Sofia, 1126, Bulg.
SOURCE:                   Biotechnology Techniques (1996), 10(10), 727-730
                          CODEN: BTECE6; ISSN: 0951-208X
PUBLISHER:                Chapman and Hall
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
GI
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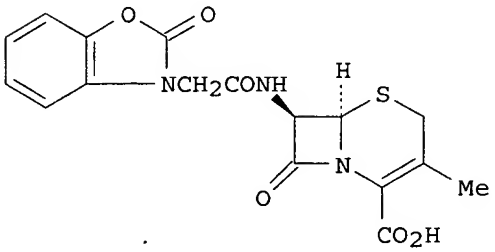
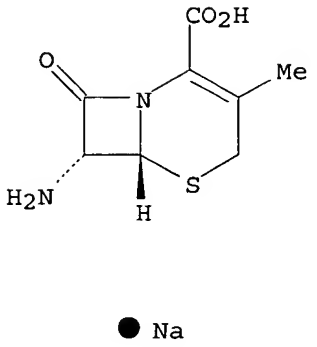


I

AB Penicillin amidase (EC 3.5.1.11) catalyzed the synthesis of cephem 7-(2-benzoxazolon-3-ylacetamido)desacetoxycephalosporanic acid (BOADCA) (I) by a kinetically controlled transfer of the non-specific 2-benzoxazolon-3-yl acetyl moiety from its polyethyleneglycol ester (m.w. 400, nine monomeric units) in the nucleophile 7-aminodesacetoxycephalosporanic acid. Penicillin amidase from E. Coli **immobilized** in polyacrylamide gel was used as biocatalyst. A high degree of nucleophile conversion (98%) into the corresponding cephem at biotechnol. relevant concns. (50 mM) was achieved.

Searched by Barb O'Bryen, STIC 2-2518

RX(1) OF 1 **A** + B ===> **C**



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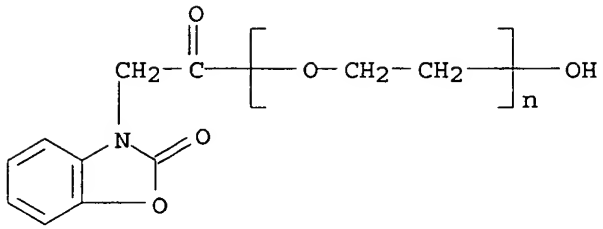

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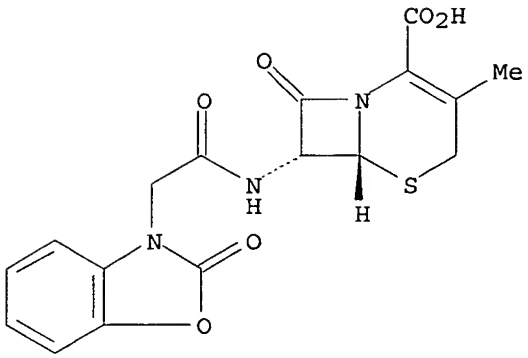

C
YIELD 77%

RX(1) RCT A **56871-82-0**, B 157168-22-4
PRO C **130970-57-9**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 18 hours, 25 deg C, pH 6.8
NTE biotransformation, enzymic, solid-supported

AB Penicillin amidase (EC 3.5.1.11) catalyzed the synthesis of cephem 7-(2-benzoxazolon-3-ylacetamido)desacetoxycephalosporanic acid (BOADCA) (I) by a kinetically controlled transfer of the non-specific 2-benzoxazolon-3-yl acetyl moiety from its polyethyleneglycol ester (m.w. 400, nine monomeric units) in the nucleophile 7-aminodesacetoxycephalosporanic acid. Penicillin amidase from E. Coli **immobilized** in polyacrylamide gel was used as biocatalyst. A high degree of nucleophile conversion (98%) into the corresponding cephem at

biotechnol. relevant concns. (50 mM) was achieved.

L37 ANSWER 2 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 142:112581 CASREACT
TITLE: Process for the preparation of cephradine
INVENTOR(S): Lenhardt, Carlos Enrique; Moody, Harold Monro; Van Dooren, Theodorus Johannes Godfried Maria; Heemskerk, Dennis; Hogenboom, Anja Gerarda Margaretha
PATENT ASSIGNEE(S): DSM IP Assets B. V., Neth.
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005003367	A2	20050113	WO 2004-EP7291	20040701
WO 2005003367	A3	20050526		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1641933	A2	20060405	EP 2004-740631	20040701
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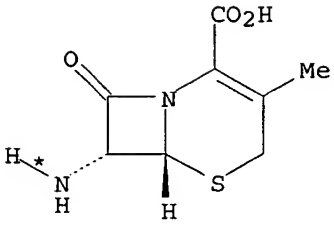
BR 2004012302	A	20060613	BR 2004-12302	20040701
CN 1813069	A	20060802	CN 2004-80018394	20040701
US 2006189802	A1	20060824	US 2006-562345	20060207
PRIORITY APPLN. INFO.:			EP 2003-77102	20030703
			EP 2003-104445	20031128
			WO 2004-EP7291	20040701

AB The present invention describes a process for preparing cephradine (I), said process comprising reacting 7-aminodesacetoxycephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form (DHa) in the presence of an enzyme in a reaction mixture to form I, resulting in a conversion of 7-ADCA into I of ≥70%, wherein the concentration D-dihydrophenylglycine (DH) in the reaction mixture is <2 weight%, wherein the conversion of 7-ADCA into I equals .apprx.100%. The invention also describes a process for the preparation of I hydrate characterized in that the process comprises reacting 7-ADCA with DHa in the presence of an enzyme in a reaction mixture to form I, preparing an aqueous solution comprising at least part of the I, and crystallizing the I from said aqueous solution The invention further describes I hydrate obtainable by a process according to invention. The invention also describes I hydrate with an absorbance at 450 nm of <0.050.

RX(1) OF 3 **A** + B ===> **C**



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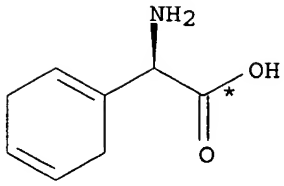

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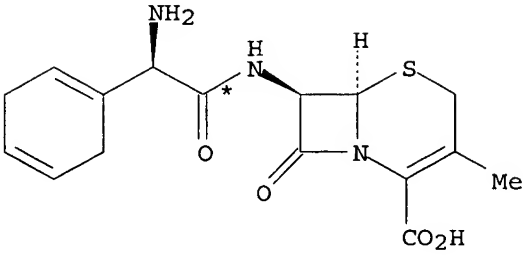


C

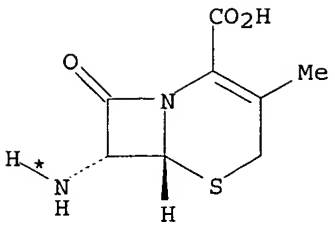
RX(1) RCT A **22252-43-3**, B 26774-88-9

STAGE(1)
RGT D 7631-90-5 NaHSO3
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 10 deg C

STAGE(2)
RGT E 1336-21-6 NH4OH
SOL 7732-18-5 Water
CON SUBSTAGE(1) 90 minutes, 10 deg C, pH 7.2
SUBSTAGE(2) 40 minutes, 10 deg C, pH 7.2 -> 7.5

PRO C **38821-53-3**
NTE biotransformation, buffered solution, enzymic, solid-supported catalyst, stereoselective, **immobilized** wild-type Pen-G acylase used as catalyst

RX(2) OF 3 **A** + B ===> **C**



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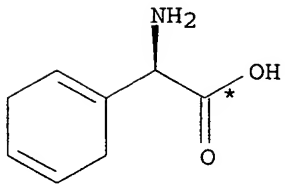

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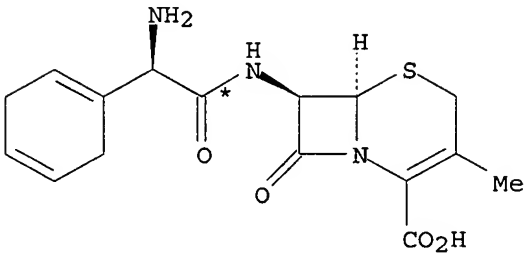


C

RX(2) RCT A **22252-43-3**, B 26774-88-9

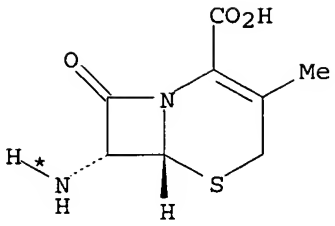
STAGE(1)
RGT D 7631-90-5 NaHSO3
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 7 deg C

STAGE(2)
RGT E 1336-21-6 NH4OH
SOL 7732-18-5 Water
CON 7 deg C, pH 8

STAGE(3)
RGT H 7664-93-9 H2SO4
SOL 7732-18-5 Water
CON 344 minutes, 7 deg C, pH 8.2

PRO C **38821-53-3**
NTE biotransformation, buffered solution, enzymic, solid-supported catalyst, stereoselective, **immobilized** Pen-G acylase mutant Phe-24-Ala used as catalyst

RX(3) OF 3 **A** + B ===> **C**



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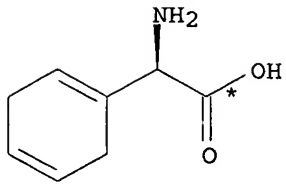

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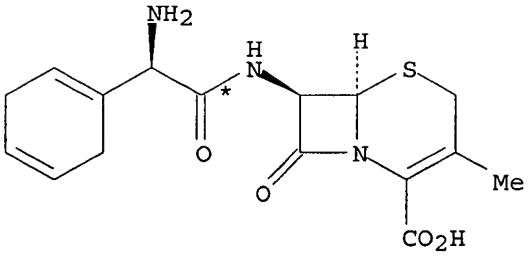


C

RX(3) RCT A **22252-43-3**

STAGE(1)
RGT D 7631-90-5 NaHSO3
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 20 deg C

STAGE(2)
RGT I 60-00-4 EDTA, E 1336-21-6 NH4OH
SOL 7732-18-5 Water
CON 5 minutes, 20 deg C, pH 6.9

STAGE(3)
RCT B 26774-88-9
RGT E 1336-21-6 NH4OH
SOL 7732-18-5 Water
CON SUBSTAGE(1) 240 minutes, 20 deg C, pH 6.9
SUBSTAGE(2) 30 minutes, 20 deg C, pH 6.9 -> 7
SUBSTAGE(3) 80 minutes, 20 deg C, pH 7 -> 7.1

PRO C **38821-53-3**
NTE biotransformation, buffered solution, enzymic, solid-supported catalyst, stereoselective, **immobilized** Pen-G acylase mutant Phe-24-Ala used as catalyst

L37 ANSWER 3 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 143:324825 CASREACT
TITLE: Synthesis of cephalexin in organic medium at high substrate concentrations and low enzyme to substrate

Searched by Barb O'Bryen, STIC 2-2518

ratio

AUTHOR(S): Illanes, A.; Altamirano, C.; Fuentes, M.; Zamorano, F.; Aguirre, C.

CORPORATE SOURCE: School of Biochemical Engineering, Pontificia Universidad Catolica Valparaiso, Valparaiso, 4059, Chile

SOURCE: Journal of Molecular Catalysis B: Enzymatic (2005), 35(1-3), 45-51
CODEN: JMCEF8; ISSN: 1381-1177

PUBLISHER: Elsevier B.V.

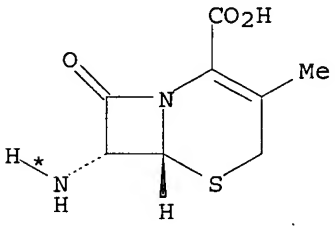
DOCUMENT TYPE: Journal

LANGUAGE: English

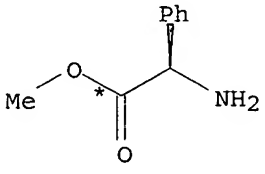
AB The kinetically controlled synthesis of cephalexin (CEX) in ethylene glycol (EG) was previously optimized at moderate substrate concns. and high enzyme to substrate ratio, obtaining yields close to stoichiometric. However, substrate concns. were low and enzyme loads high enough for production purpose. The synthesis of cephalexin in 40% (volume/volume) ethylene glycol at 20 °C and pH 7.0 with glyoxyl-agarose **immobilized** penicillin acylase (GAPA) was studied at high substrates concns. to the point of saturation and beyond. Phenylglycine Me ester (PGME) was the acyl donor at a molar ratio of 3 with respect to nucleophile. At initially homogeneous conditions with nucleophile concentration close to its solubility and at low enzyme to substrate ratio, productivity increase eight times and specific productivity five times with respect to a control at moderate substrates concns. and high enzyme to substrate ratio. At initially heterogeneous conditions with partially undissolved nucleophile and low enzyme to substrate ratio, increases in productivity and specific productivity were eleven and seven times, resp. The biocatalyst was very stable under reaction conditions, so that a very high global productivity is anticipated, making the enzymic process competitive with existing chemical synthesis.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 **A** + B ===> **C**

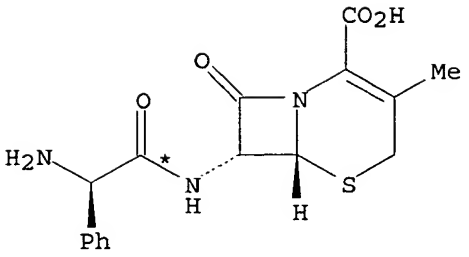


A



B

(1) ⟶



C

RX(1) RCT A **22252-43-3**, B 24461-61-8
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 107-21-1 (CH2OH)2, 7732-18-5 Water
CON 20 deg C, pH 7.0
NTE biotransformation, enzymic, Penicillin acylase from recombinant Escherichia coli, catalyst on glyoxyl-agarose, optimization study, optimized on stoichiometry,concentration

AB The kinetically controlled synthesis of cephalexin (CEX) in ethylene glycol (EG) was previously optimized at moderate substrate concns. and high enzyme to substrate ratio, obtaining yields close to stoichiometric. However, substrate concns. were low and enzyme loads high enough for production purpose. The synthesis of cephalexin in 40% (volume/volume) ethylene glycol at 20 °C and pH 7.0 with glyoxyl-agarose **immobilized** penicillin acylase (GAPA) was studied at high substrates concns. to the point of saturation and beyond. Phenylglycine Me ester (PGME) was the acyl donor at a molar ratio of 3 with respect to nucleophile. At initially homogeneous conditions with nucleophile concentration close to its solubility and at low enzyme to substrate ratio, productivity increase eight times and specific productivity five times with respect to a control at moderate substrates concns. and high enzyme to substrate ratio. At initially heterogeneous conditions with partially undissolved nucleophile and low enzyme to substrate ratio, increases in productivity and specific productivity were eleven and seven times, resp. The biocatalyst was very stable under reaction conditions, so that a very high global productivity is anticipated, making the enzymic process competitive with existing chemical synthesis.

IT **Immobilization**, molecular or cellular
(enzyme; synthesis of cephalexin in organic medium at high substrate concns. and low enzyme to substrate ratio)

L37 ANSWER 4 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:122419 CASREACT
TITLE: Process for enzymatic synthesis of β-lactam antibiotics
INVENTOR(S): Linda, Paolo; Gardossi, Lucia; Toniutti, Micaela
PATENT ASSIGNEE(S): Universita' Degli Studi Di Trieste, Italy
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

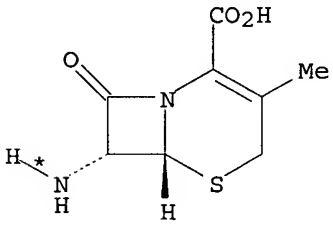
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004062558	A2	20040729	WO 2004-EP182	20040114
WO 2004062558	A3	20050609		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ

PRIORITY APPLN. INFO.: IT 2003-MI42 20030114

AB The present invention describes a process for the preparation of β-lactam antibiotics, cephalexin and ampicillin, wherein the β-lactam nucleus is acylated with an acylating agent, D-phenylglycine, by means of a reaction biocatalyzed by a catalytic enzyme. The acylation reaction is carried out in solid phase in solvent free systems (water or organic solvents) for the dispersion of reagents and at controlled temps.

RX(3) OF 6 ...**G** + 4 B ===> **H** + I + J



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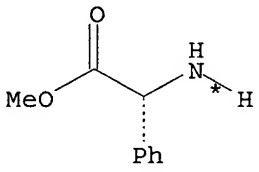

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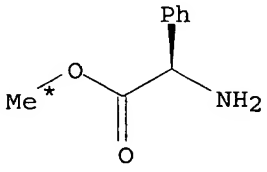

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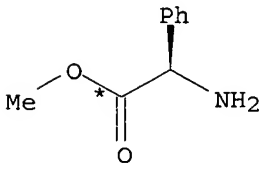
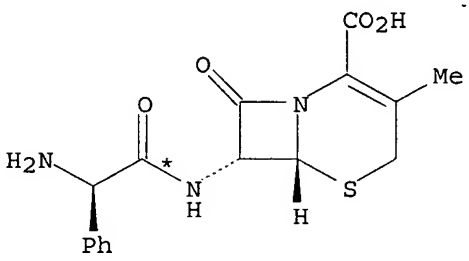
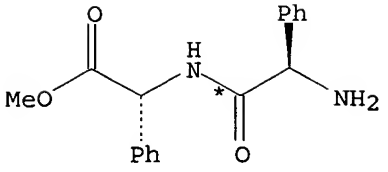


2 B

(3)



H



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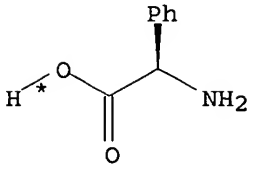
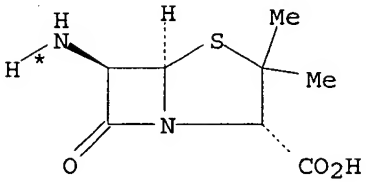


J

RX(3) RCT G **22252-43-3**, B 24461-61-8
PRO H **15686-71-2**, I 722547-49-1, J 875-74-1
CAT **9014-06-6** Penicillin amidase
CON 3 hours, room temperature
NTE biotransformation, enzymic, no solvent, optimization study, solid-supported catalyst, stereoselective, penicillin G. acylase from E. coli **immobilized** on solid **polymer** used as catalyst

RX(4) OF 6 ...L + 4 B ===> I + J + M



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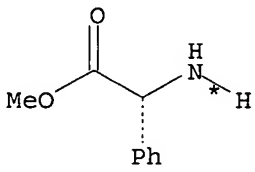

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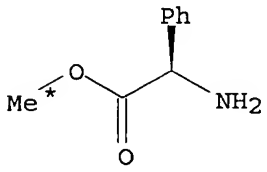

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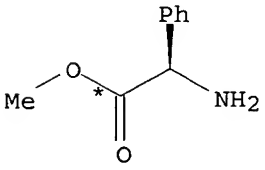
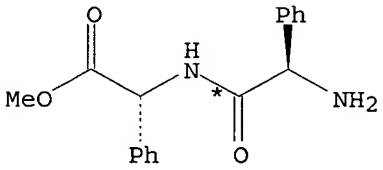


2 B

(4)



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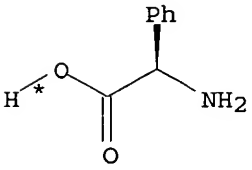

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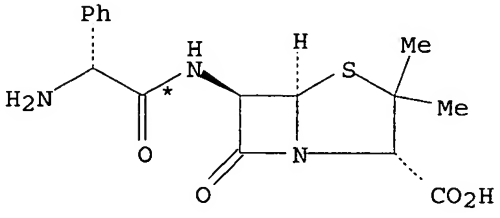
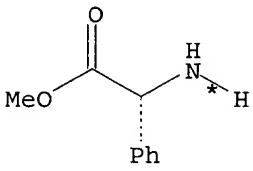


M

Searched by Barb O'Bryen, STIC 2-2518

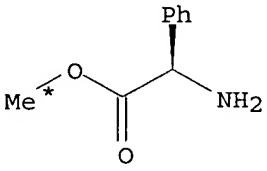
RX(4) RCT L 551-16-6, B 24461-61-8
PRO I 722547-49-1, J 875-74-1, M 69-53-4
CAT **9014-06-6** Penicillin amidase
CON room temperature
NTE biotransformation, enzymic, no solvent, optimization study, solid-supported catalyst, stereoselective, penicillin G. acylase from E. coli **immobilized** on solid **polymer** used as catalyst

RX(5) OF 6 COMPOSED OF RX(1), RX(3)
RX(5) 4 A + **G** ===> **H** + I + J



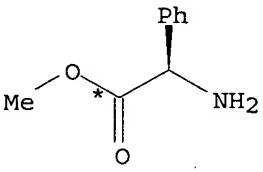
● HCl

A



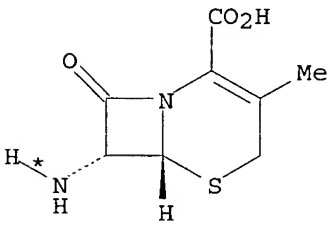
● HCl

A



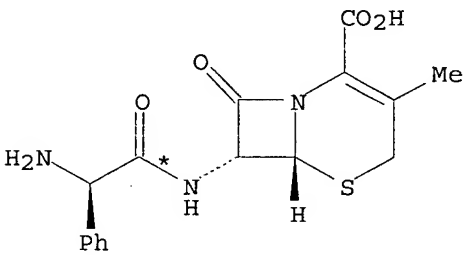
● HCl

2 A

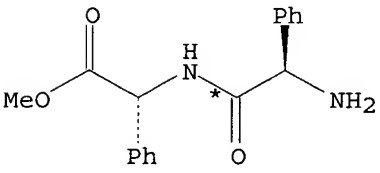


G

2 STEPS ⟶



H



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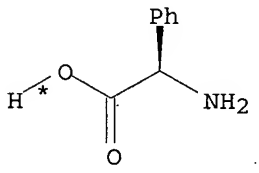


J

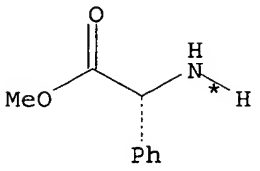
RX(1) RCT A 19883-41-1
RGT C 6132-02-1 Carbonic acid disodium salt, decahydrate
PRO B 24461-61-8
SOL 75-09-2 CH2Cl2

Searched by Barb O'Bryen, STIC 2-2518

CON room temperature

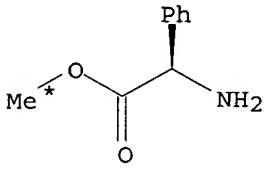
RX(3) RCT G **22252-43-3**, B 24461-61-8
PRO H **15686-71-2**, I 722547-49-1, J 875-74-1
CAT **9014-06-6** Penicillin amidase
CON 3 hours, room temperature
NTE biotransformation, enzymic, no solvent, optimization study, solid-supported catalyst, stereoselective, penicillin G. acylase from E. coli **immobilized** on solid **polymer** used as catalyst

RX(6) OF 6 COMPOSED OF RX(1), RX(4)
RX(6) 4 A + L ===> I + J + M



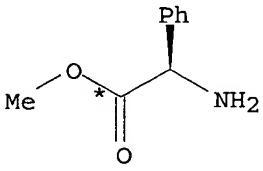
● HCl

A



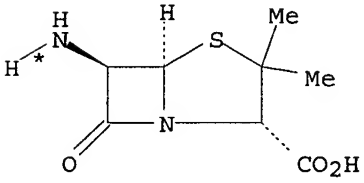
● HCl

A



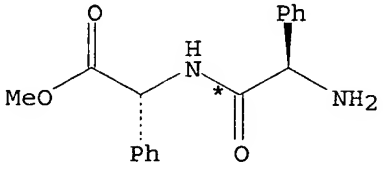
● HCl

2 A

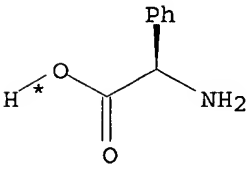


L

2 STEPS



I



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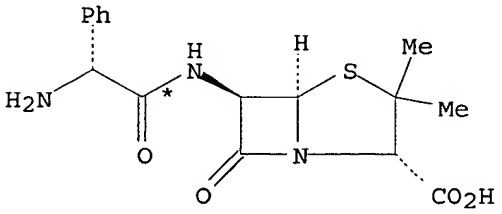

M

RX(1) RCT A 19883-41-1
RGT C 6132-02-1 Carbonic acid disodium salt, decahydrate
PRO B 24461-61-8

Searched by Barb O'Bryen, STIC 2-2518

SOL 75-09-2 CH2Cl2
CON room temperature

RX(4) RCT L 551-16-6, B 24461-61-8
PRO I 722547-49-1, J 875-74-1, M 69-53-4
CAT **9014-06-6** Penicillin amidase
CON room temperature
NTE biotransformation, enzymic, no solvent, optimization study, solid-supported catalyst, stereoselective, penicillin G. acylase from E. coli **immobilized** on solid **polymer** used as catalyst

IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**immobilized**; process for enzymic synthesis of β-lactam antibiotics)

L37 ANSWER 5 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 140:390367 CASREACT
TITLE: Simple enzymatic process for preparing cefazolin
INVENTOR(S): Sanchez Ferrer, Alvaro; Garcia Carmona, Francisco
PATENT ASSIGNEE(S): Bioferma Murcia, S.A., Spain
SOURCE: Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1416054	A1	20040506	EP 2002-380224	20021031
EP 1416054	B1	20050817		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
AT 302283	E	20050915	AT 2002-380224	20021031
WO 2004039997	A1	20040513	WO 2003-EP12165	20031030
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003282071	A1	20040525	AU 2003-282071	20031030
EP 1556500	A1	20050727	EP 2003-773688	20031030
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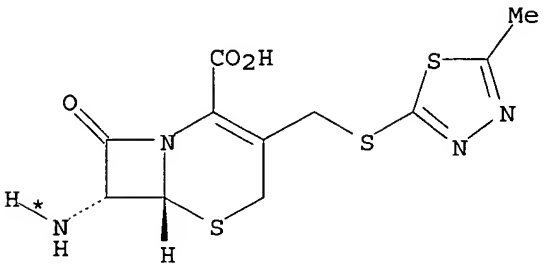
PRIORITY APPLN. INFO.: EP 2002-380224 20021031
WO 2003-EP12165 20031030

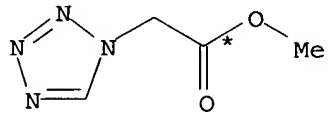
AB Aprocess is provided for the enzymic preparation of cefazolin (7-(1-H-tetrazol-1-yl) acetamide-3-(2-methyl-1,3,4-thiadiazol-5-yl)thiomethyl-3-cephem-4-carboxylic acid) by the acylation of 7-amino-3-[5-methyl-(1,3,4-thiadiazol-2-yl)thiomethyl]-3-cephem-4-carboxylic acid by penicillin G amidase with 1H-tetrazole-1-acetic acid or its derivs. The process is distinguished by the ability to use crude

reactants and still obtain high yields of product.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(2) OF 4 ...**F** + C ===> **G**

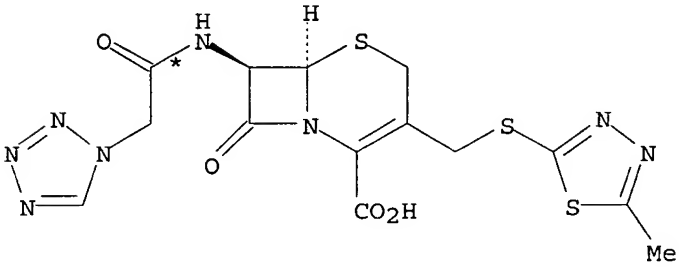


F
salts



C

(2) →



G
YIELD 88%

RX(2) RCT F **30246-33-4D**

STAGE(1)
RGT H 7722-76-1 (NH4)H2PO4
SOL 7732-18-5 Water
CON 25 deg C, pH 8.6

STAGE(2)
RGT I 7664-38-2 H3PO4
SOL 7732-18-5 Water
CON 25 deg C, pH 8.6 -> 7.5

STAGE(3)
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 4 deg C

STAGE(4)
RCT C 55633-19-7
RGT J 7664-41-7 NH3

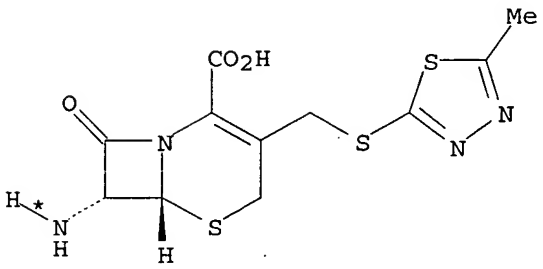
Searched by Barb O'Bryen, STIC 2-2518

SOL 7732-18-5 Water
CON 105 minutes, 4 deg C, pH 7.5

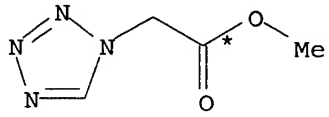
STAGE(5)
RGT K 7647-01-0 HCl
SOL 7732-18-5 Water
CON 2 hours, 4 deg C, pH 1.5

PRO G **25953-19-9**
NTE biotransformation, buffered solution, enzymic, solid-supported catalyst, penicillin G amidase from Escherichia coli **immobilized** on macroporous beads used as catalyst

RX(3) OF 4 **F** + C ===> **G**

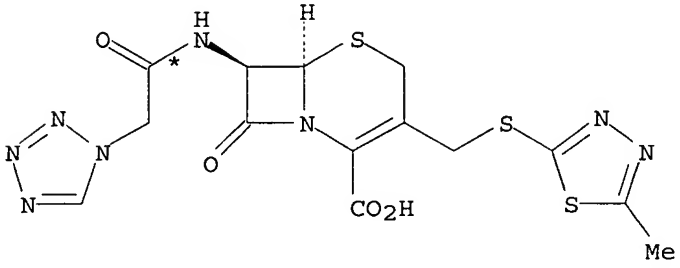


F
salts



C

(3) ⟶



G

RX(3) RCT F **30246-33-4D**

STAGE(1)
RGT H 7722-76-1 (NH4)H2PO4
SOL 7732-18-5 Water
CON 25 deg C, pH 8.6

STAGE(2)
RGT I 7664-38-2 H3PO4
SOL 7732-18-5 Water
CON 25 deg C, pH 8.6 -> 7.5

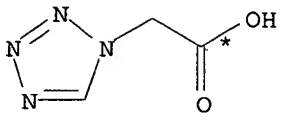
STAGE(3)
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 4 deg C

STAGE(4)
RCT C 55633-19-7
RGT J 7664-41-7 NH3
SOL 7732-18-5 Water
CON 105 minutes, 4 deg C, pH 7.5

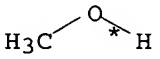
STAGE(5)
RGT K 7647-01-0 HCl
SOL 7732-18-5 Water
CON 2 hours, 4 deg C, pH 1.5

PRO G **25953-19-9**
NTE biotransformation, buffered solution, enzymic, soluble penicillin G amidase from Escherichia coli without **immobilization** used as catalyst

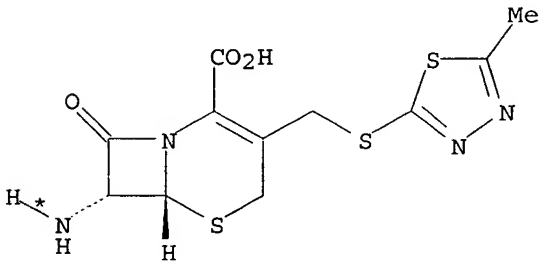
RX(4) OF 4 COMPOSED OF RX(1), RX(2)
RX(4) A + B + **F** ===> **G**



A



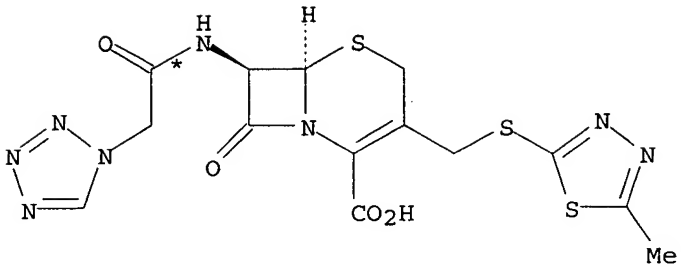
B



F
salts

2
STEPS

Searched by Barb O'Bryen, STIC 2-2518



G
YIELD 88%

RX(1) RCT A 21732-17-2, B 67-56-1

STAGE(1)
RGT D 7664-93-9 H2SO4
SOL 67-56-1 MeOH
CON 3 hours, reflux

STAGE(2)
RGT E 144-55-8 NaHCO3
CON room temperature, neutralized

PRO C 55633-19-7

RX(2) RCT F **30246-33-4D**

STAGE(1)
RGT H 7722-76-1 (NH4)H2PO4
SOL 7732-18-5 Water
CON 25 deg C, pH 8.6

STAGE(2)
RGT I 7664-38-2 H3PO4
SOL 7732-18-5 Water
CON 25 deg C, pH 8.6 -> 7.5

STAGE(3)
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 4 deg C

STAGE(4)
RCT C 55633-19-7
RGT J 7664-41-7 NH3
SOL 7732-18-5 Water
CON 105 minutes, 4 deg C, pH 7.5

STAGE(5)
RGT K 7647-01-0 HCl
SOL 7732-18-5 Water
CON 2 hours, 4 deg C, pH 1.5

PRO G **25953-19-9**
NTE biotransformation, buffered solution, enzymic, solid-supported

catalyst, penicillin G amidase from Escherichia coli **immobilized** on macroporous beads used as catalyst

IT **Immobilization**, molecular or cellular
(enzyme; simple enzymic process for preparing cefazolin)

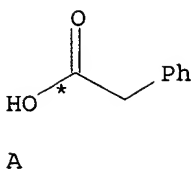
IT Enzymes, preparation
RL: BCP (Biochemical process); CAT (Catalyst use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**immobilized**; simple enzymic process for preparing cefazolin)

L37 ANSWER 6 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:172923 CASREACT
TITLE: Encapsulation of crosslinked penicillin G acylase aggregates in LentiKats: Evaluation of a novel biocatalyst in organic media
AUTHOR(S): Wilson, Lorena; Illanes, Andres; Pessela, Benevides C. C.; Abian, Olga; Fernandez-Lafuente, Roberto; Guisan, Jose M.
CORPORATE SOURCE: Departamento de Biocatalisis, Instituto de Catalisis, Madrid, 28049, Spain
SOURCE: Biotechnology and Bioengineering (2004), 86(5), 558-562
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

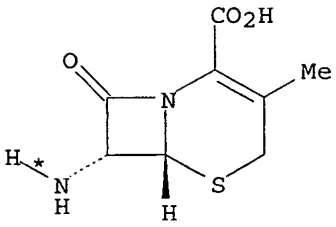
AB The encapsulation of crosslinked enzyme aggregates (CLEA) of penicillin G acylase into a very rigid **polymeric** matrix based on polyvinyl alc. (LentiKats) has been used successfully to improve the inadequate mech. properties of CLEA. This encapsulation decreased CLEA activity by only around 40%. As compensation, a significant improvement in the stability of the CLEA in the presence of organic solvents was detected. This could be related to the highly hydrophilic environment inside the LentiKats biocatalysts: Partition expts. showed that the concentration of dioxane inside LentiKats was lower than in the reaction medium. In fact, thermal stability was about the same as in the corresponding CLEA. This permitted great improvement in the reaction rate for thermodynamically controlled synthesis of a model antibiotic (using phenylacetic acid and 7-amino-deacetoxycephalosporanic acid). Even more importantly, yields could be improved by using LentiKats-encapsulated CLEA, very likely by a favorable product/substrate partition. Thus, this very simple technique not only provides an efficient technique for solving the mech. stability problem associated with CLEA, but also greatly improves the behavior of CLEA in organic media.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 A + **B** ===> **C**

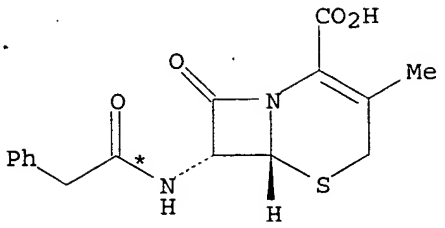


A



B

(1) →



C
YIELD 55%

RX(1) RCT A 103-82-2, B **22252-43-3**
PRO C **27255-72-7**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water, 123-91-1 Dioxane
CON 15 hours, 4 deg C, pH 7
NTE biotransformation, buffered solution, enzymic, phosphate, cross-linked enzyme aggregate of penicillin G acylase **immobilized** in LentiKats matrix used, solvent, temperature, and mechanical stability of biocatalyst improved by encapsulation in polyvinyl alcohol beads

AB The encapsulation of crosslinked enzyme aggregates (CLEA) of penicillin G acylase into a very rigid **polymeric** matrix based on polyvinyl alc. (LentiKats) has been used successfully to improve the inadequate mech. properties of CLEA. This encapsulation decreased CLEA activity by only around 40%. As compensation, a significant improvement in the stability of the CLEA in the presence of organic solvents was detected. This could be related to the highly hydrophilic environment inside the LentiKats biocatalysts: Partition expts. showed that the concentration of dioxane inside LentiKats was lower than in the reaction medium. In fact, thermal stability was about the same as in the corresponding CLEA. This permitted great improvement in the reaction rate for thermodynamically controlled synthesis of a model antibiotic (using phenylacetic acid and 7-amino-deacetoxycephalosporanic acid). Even more importantly, yields could be improved by using LentiKats-encapsulated CLEA, very likely by a favorable product/substrate partition. Thus, this very simple technique not only provides an efficient technique for solving the mech. stability problem associated with CLEA, but also greatly improves the behavior of CLEA in organic media.

IT **Immobilization**, molecular or cellular
(enzyme; encapsulation of crosslinked penicillin G acylase aggregates in LentiKats)

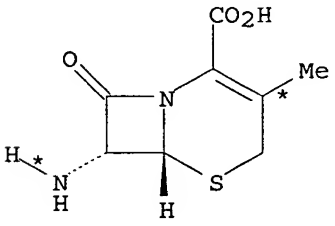
L37 ANSWER 7 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:70302 CASREACT
TITLE: Semi-continuous enzymatic synthesis of cefaclor enhanced by in situ product removal
AUTHOR(S): Yang, Liu; Wei, Dongzhi; Zhang, Yewang
CORPORATE SOURCE: State Key Laboratory of Bioreactor Engineering, New World Institute of Biotechnology, East China University of Science and Technology, Shanghai, 200237, Peop. Rep. China
SOURCE: Journal of Chemical Technology and Biotechnology (2004), 79(5), 480-485
CODEN: JCTBED; ISSN: 0268-2575
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Enzymic synthesis of cefaclor was carried out with kinetic control. The product yield was improved by the continuous removal of product from the reaction mixture via complexation of cefaclor with 1-naphthol. The effects of pH and temperature on the enzymic and complexing reactions were investigated.

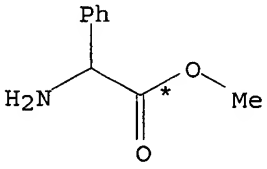
The efficiency of the enzymic conversion of cefaclor in the complexing reaction was 80% under optimum reaction conditions. In situ product removal (ISPR) decreased product concentration in the bioreactor, consequently the yield of cefaclor increased from 57% (without ISPR) to 80% (with ISPR). The specially designed reactor allowed enzymic reaction and product removal to be accomplished simultaneously, in which the productivity of cefaclor was improved to 65 g dm-3 by semi-continuous operation lasting for 55 h.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 2 **A** + 2 B ===> **C** + D

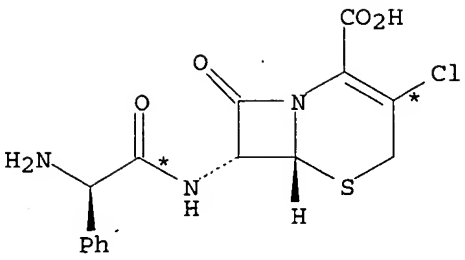


A

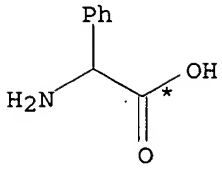


2 B

(1) →



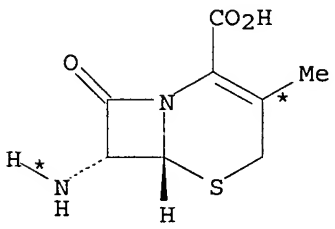
C
YIELD 57%



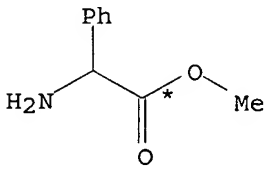
D

RX(1) RCT A **22252-43-3**, B 26682-99-5
PRO C **53994-73-3**, D 2835-06-5
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 7 hours, 10 deg C, pH 6.5
NTE biotransformation; enzymic; penicillin G acylase from Bacillus megaterium **immobilized** on epoxyacrylic **resin** used; optimization study; optimized on temp., pH

RX(2) OF 2 **A** + 2 B ===> **C** + D

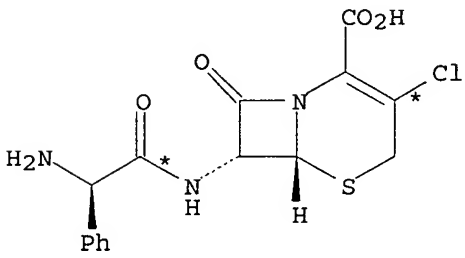


A

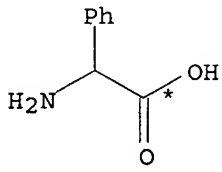


2 B

(2) ⟶



C
YIELD 80%



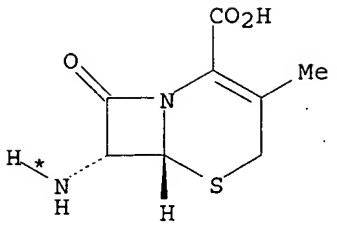
D

RX(2) RCT A **22252-43-3**, B 26682-99-5
RGT G 90-15-3 1-Napthol
PRO C **53994-73-3**, D 2835-06-5

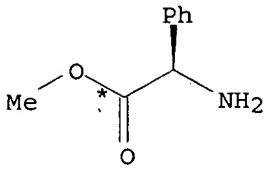
CAT 9014-06-6 Penicillin amidase
SOL 7732-18-5 Water
CON 55 hours, 10 deg C, pH 6.5
NTE biotransformation; enzymic; penicillin G acylase from Bacillus megaterium **immobilized** on epoxyacrylic **resin** used; phosphate buffered soln.; yield increased by in situ product removal by complexation with 1-naphthol

L37 ANSWER 8 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:105308 CASREACT
TITLE: Optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temperatures
AUTHOR(S): Illanes, A.; Anjari, M. S.; Altamirano, C.; Aguirre, C.
CORPORATE SOURCE: School of Biochemical Engineering, Pontificia Universidad Catolica Valparaiso, Valparaiso, 2147, Chile
SOURCE: Journal of Molecular Catalysis B: Enzymatic (2004), 30(2), 95-103
CODEN: JMCEF8; ISSN: 1381-1177
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Organic cosolvents, and among them, polyols, are suitable media to perform the enzymic synthesis of β-lactam antibiotics with **immobilized** penicillin acylase, because they effectively reduce water activity, depressing hydrolytic reactions in favor of synthesis. Among polyols, ethylene glycol has proven to be particularly suited as reaction medium for their synthesis. Previous studies have shown that pH, temperature, and cosolvent concentration are the most relevant variables in the kinetically controlled synthesis of cephalexin from 7-amino-3-deacetoxy cephalosporanic acid and phenylglycine Me ester, conversion yield increasing at low temps. and high cosolvent concns. The objective of this work is the optimization of temperature, pH, and ethylene glycol concentration in the kinetically controlled synthesis of cephalexin with **immobilized** penicillin acylase at lower than ambient temperature in terms of substrate molar conversion yield. Phenylglycine was used as acyl donor and 7-amino-3-deacetoxy cephalosporanic acid was the limiting substrate at 30 mM. Optimization was performed using surface of response methodol., optimum conditions being 12 °C, pH 6.8, and 60% (volume/volume) ethylene glycol, at which cephalexin yield was close to stoichiometric with respect to the limiting nucleophile, which is unattainable in aqueous medium. Stability of the biocatalyst at optimum conditions for cephalexin synthesis was very high, with a projected half-life of 1500 h, making it a suitable catalyst for the large-scale production of cephalexin.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 **A** + B ===> **C**

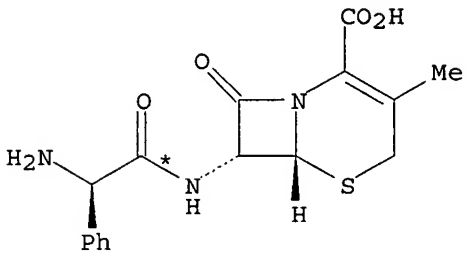


A



B

(1) →



C
YIELD 100%

RX(1) RCT A **22252-43-3**, B 24461-61-8
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 107-21-1 (CH2OH)2, 7732-18-5 Water
CON 2 hours, 12.5 deg C, 6.75 atm
NTE biotransformation; enzymic; **immobilized** penicillin acylase from Escherichia coli used; optimization study; optimized on pH, temp., solvent compn., stoichiometry

TI Optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temperatures

AB Organic cosolvents, and among them, polyols, are suitable media to perform the enzymic synthesis of β-lactam antibiotics with **immobilized** penicillin acylase, because they effectively reduce water activity, depressing hydrolytic reactions in favor of synthesis. Among polyols, ethylene glycol has proven to be particularly suited as reaction medium for their synthesis. Previous studies have shown that pH, temperature, and cosolvent concentration are the most relevant variables in the kinetically controlled synthesis of cephalexin from 7-amino-3-deacetoxy cephalosporanic acid and phenylglycine Me ester, conversion yield increasing at low temps. and high cosolvent concns. The objective of this work is the optimization of temperature, pH, and ethylene glycol concentration in the kinetically controlled synthesis of cephalexin with **immobilized** penicillin acylase at lower than ambient temperature in terms of substrate molar conversion yield. Phenylglycine was used as acyl donor and 7-amino-3-deacetoxy cephalosporanic acid was the limiting substrate at 30 mM. Optimization was performed using surface of response methodol., optimum conditions being 12 °C, pH 6.8, and 60% (volume/volume) ethylene glycol, at which cephalexin yield was close to stoichiometric

with respect to the limiting nucleophile, which is unattainable in aqueous medium. Stability of the biocatalyst at optimum conditions for cephalexin synthesis was very high, with a projected half-life of 1500 h, making it a suitable catalyst for the large-scale production of cephalexin.

IT Reaction kinetics
(biochem.; optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT pH
(biol. effects of; optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT Acylation
(enzymic; optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**immobilized**; optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT Temperature effects, biological
(optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT Optimization
(statistical; optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT 107-21-1, Ethylene glycol, processes
RL: BCP (Biochemical process); BIOL (Biological study); PROC (Process)
(optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT 9014-06-6, Penicillin acylase
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT 22252-43-3, 7-Amino-3-deacetoxy cephalosporanic acid 24461-61-8, R-Phenylglycine methyl ester
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

IT 15686-71-2P, Cephalexin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(optimization of cephalexin synthesis with **immobilized** penicillin acylase in ethylene glycol medium at low temps.)

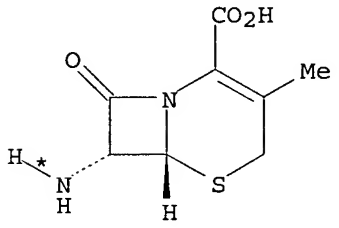
L37 ANSWER 9 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:122372 CASREACT
TITLE: Biosynthesis of cephalexin in PEG400-ammonium sulfate and PEG400-magnesium sulfate aqueous two-phase systems
AUTHOR(S): Cao, Xuejun; Zhu, Jianhang; Wei, Dongzhi; Hur, Byung-Ki
CORPORATE SOURCE: State Key Laboratory of Bioreactor Engineering, Department of Biochemical Engineering, East China University of Science and Technology, Shanghai, 200237, Peop. Rep. China

SOURCE: Journal of Microbiology and Biotechnology (2004), 14(1), 62-67
CODEN: JOMBES; ISSN: 1017-7825
PUBLISHER: Korean Society for Microbiology and Biotechnology
DOCUMENT TYPE: Journal
LANGUAGE: English

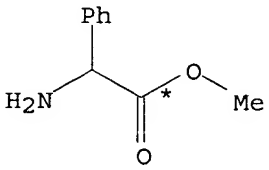
AB The biosynthesis of cephalexin was carried out in the aqueous two-phase systems using penicillin acylase as a catalyst, and 7-aminodeacetoxycephalosporanic acid (7-ADCA) and phenylglycine Me ester (PGME), as substrates. 20% PEG400-17.5% (NH4)2SO4 containing 0.5 M NaCl and 1.5 M methanol aqueous two-phase systems (ATPS) were selected as reaction medium, and 53% product yield was obtained using **immobilized** penicillin acylase as a catalyst. 20% PEG400-15% MgSO4 ATPS was also used for the synthesis of cephalexin, and 60-62% product yield was obtained by using free penicillin acylase as a catalyst. When batch reactions were repeated in the ATPS, the cephalexin yields decreased during the reactions due to deactivation, loss, and product inhibition of penicillin acylase. The effect of different ratio of phenylglycine Me ester to 7-ADCA on the product yield was investigated, and high cephalexin yield was obtained at a high molar ratio.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 3 **A** + **B** ===> **C**



A



B

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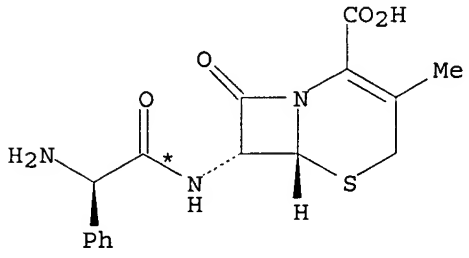
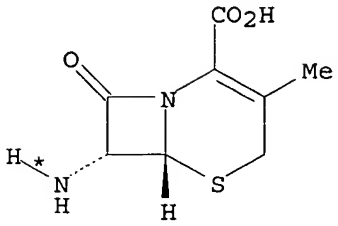


C
YIELD 53%

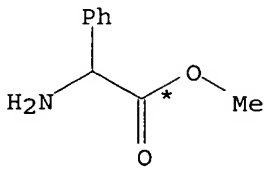
RX(1) RCT A **22252-43-3**, B 26682-99-5
RGT D 25322-68-3 HOCH2CH2OH polymer, E 7783-20-2 (NH4)2SO4, F 7632-05-5 Na orthophosphate
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase

SOL 7732-18-5 Water, 67-56-1 MeOH
CON 15 deg C, pH 6.5
NTE biotransformation, enzymic, optimized on the molar ratio of the substrates

RX(2) OF 3 **A** + B ===> **C**

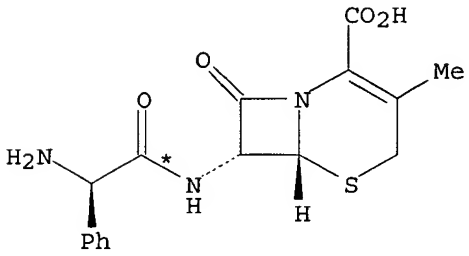


A



B

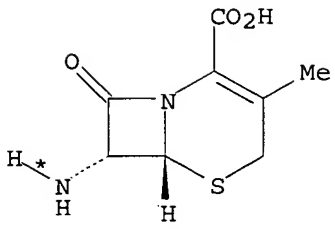
(2)



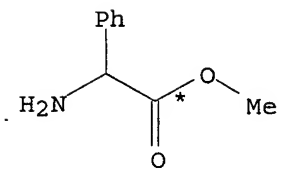
C
YIELD 60%

RX(2) RCT A **22252-43-3**, B 26682-99-5
RGT D 25322-68-3 HOCH2CH2OH polymer, J 7487-88-9 MgSO4, F 7632-05-5 Na orthophosphate
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water, 67-56-1 MeOH
CON room temperature, pH 6.5
NTE biotransformation, enzymic, optimized on the molar ratio of the substrates and on the concentration of MgSO4

RX(3) OF 3 **A** + B ===> **C**

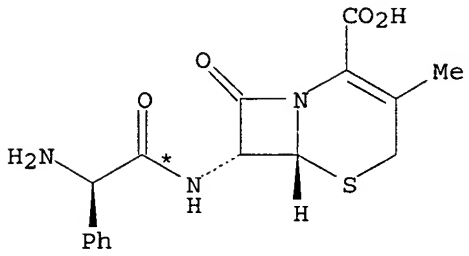


A



B

(3) →



C
YIELD 19%

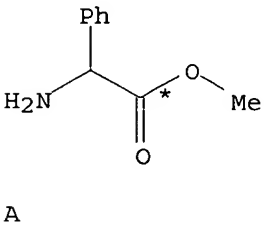
RX(3) RCT A **22252-43-3**, B 26682-99-5
RGT F 7632-05-5 Na orthophosphate
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 15 deg C, pH 6.5
NTE biotransformation, enzymic, optimized on the molar ratio of the substrates

AB The biosynthesis of cephalexin was carried out in the aqueous two-phase systems using penicillin acylase as a catalyst, and 7-aminodeacetoxycephalosporanic acid (7-ADCA) and phenylglycine Me ester (PGME), as substrates. 20% PEG400-17.5% (NH4)2SO4 containing 0.5 M NaCl and 1.5 M methanol aqueous two-phase systems (ATPS) were selected as reaction medium, and 53% product yield was obtained using **immobilized** penicillin acylase as a catalyst. 20% PEG400-15% MgSO4 ATPS was also used for the synthesis of cephalexin, and 60-62% product yield was obtained by using free penicillin acylase as a catalyst. When batch reactions were repeated in the ATPS, the cephalexin yields decreased during the reactions due to deactivation, loss, and product inhibition of penicillin acylase. The effect of different ratio of phenylglycine Me ester to 7-ADCA on the product yield was investigated, and high cephalexin yield was obtained at a high molar ratio.

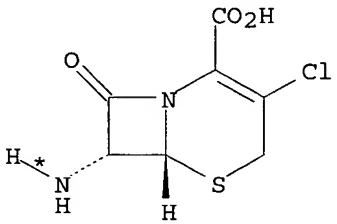
L37 ANSWER 10 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 139:322314 CASREACT
TITLE: Enhanced enzymatic synthesis of a semi-synthetic cephalosprin, cefaclor, with in situ product removal
AUTHOR(S): Yang, Liu; Wei, Dong-Zhi
CORPORATE SOURCE: New World Institute of Biotechnology, State Key

Laboratory of Bioreactor Engineering, East China University of Science and Technology, Shanghai, 200237, Peop. Rep. China
SOURCE: Biotechnology Letters (2003), 25(14), 1195-1198
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the enzymic synthesis of cefaclor, 3-chloro-7-d-(2-phenylglycinamide)-3-cephem-4-carboxylic acid, from phenylglycine Me ester and 7-aminodesacetoxymethyl-3-chlorocephalosporanic acid, the in situ product could influence both the overall conversion and hydrolysis of the ester. Optimization of the parameters, such as pH 6.2, 5°C and substrate molar ratio of 2:1, made in situ product removal improve the overall conversion from 64% to 85% (mol/mol).
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 A + **B** ===> **C**

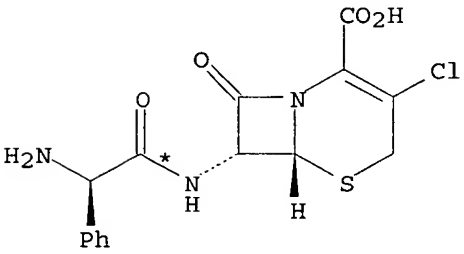


A



B

(1) →



C

RX(1) RCT A 26682-99-5, B **53994-69-7**
PRO C **53994-73-3**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 5 deg C, pH 6.2
NTE biotransformation, enzymic, Penicillin G acylase used, fixed-bed reactor, fluidized-bed bioreactor

IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)

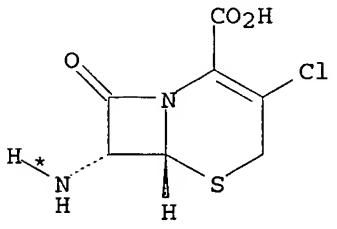
(**immobilized**; enhanced enzymic synthesis of semi-synthetic cephalosprin, cefaclor, with in situ product removal)

L37 ANSWER 11 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 139:84036 CASREACT
TITLE: Kinetically controlled synthesis of cefaclor using penicillin G acylase
AUTHOR(S): Yang, Liu; Wei, Dong-zhi; Xue, Ping; Lu, Guan-zhong
CORPORATE SOURCE: Institute of Biochemistry, East China University of Science and Technology, Shanghai, 200237, Peop. Rep. China
SOURCE: Fenzi Cuihua (2003), 17(2), 81-87
CODEN: FECUEN; ISSN: 1001-3555
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: English

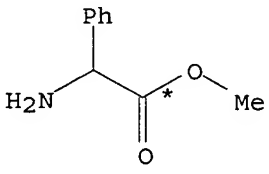
AB Enzymic synthesis of cefaclor from 7-aminodesacetoxymethyl-3-chlorocephalosporanic acid (7-ACCA) and phenylglycine derivs. using penicillin G acylase was studied. Many factors that affect the conversion of 7-ACCA to cefaclor were examined The **immobilized** enzyme from Bacillus megaterium gave better catalytic properties and higher conversion was obtained using phenylglycine Me ester (PGME) as acyl donor. And the external mass transfer limitation could be eliminated when the stirring rate was >150 rpm. Low temperature was beneficial for the synthesis and the results showed that the synthetase activity was hardly influenced by temperature while the amidase activity was affected greatly by temperature The optimum reaction conditions were determined at pH 6.5 and 10°. The best 7-ACCA conversion of 56% was achieved when the initial concentration of 7-ACCA and PGME was at 50 mM and 150 mM, resp.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 **A** + B ===> **C**

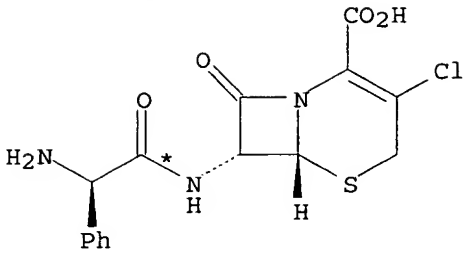


A



B

(1) →



C

RX(1) RCT A **53994-69-7**, B 26682-99-5
PRO C **53994-73-3**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON 10 deg C, pH 6.5
NTE biotransformation, enzymic, **immobilized** penicillin G acylase from Bacillus megaterium gave the best results, sodium phosphate buffered soln., optimization study

AB Enzymic synthesis of cefaclor from 7-aminodesacetoxymethyl-3-chlorocephalosporanic acid (7-ACCA) and phenylglycine derivs. using penicillin G acylase was studied. Many factors that affect the conversion of 7-ACCA to cefaclor were examined The **immobilized** enzyme from Bacillus megaterium gave better catalytic properties and higher conversion was obtained using phenylglycine Me ester (PGME) as acyl donor. And the external mass transfer limitation could be eliminated when the stirring rate was >150 rpm. Low temperature was beneficial for the synthesis and the results showed that the synthetase activity was hardly influenced by temperature while the amidase activity was affected greatly by temperature The optimum reaction conditions were determined at pH 6.5 and 10°. The best 7-ACCA conversion of 56% was achieved when the initial concentration of 7-ACCA and PGME was at 50 mM and 150 mM, resp.

IT **Immobilization**, molecular or cellular
(kinetically controlled synthesis of cefaclor using **immobilized** penicillin G acylase)

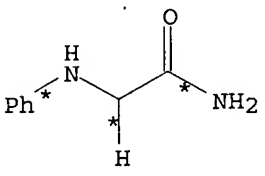
L37 ANSWER 12 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 137:309546 CASREACT
TITLE: In situ product removal during enzymatic cephalexin synthesis by complexation
AUTHOR(S): Schroen, C. G. P. H.; Nierstrasz, V. A.; Bosma, R.; Kemperman, G. J.; Strubel, M.; Ooijkaas, L. P.; Beeftink, H. H.; Tramper, J.
CORPORATE SOURCE: Department of Food Science, Biotechnion, Food and Bioprocess Engineering Group, Wageningen University, Wageningen, 6700 EV, Neth.
SOURCE: Enzyme and Microbial Technology (2002), 31(3), 264-273
CODEN: EMTED2; ISSN: 0141-0229
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In this paper, 'complexation' indicates the formation of clathrate type inclusion compds. of cephalexin with naphthalene derivs. These inclusion

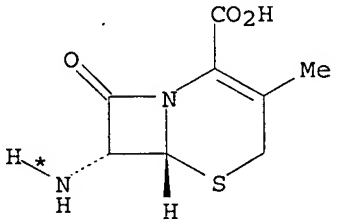
compds. readily crystallize in solution, resulting in specific co-crystals of complexing agent and cephalexin with a set ratio between both components. Complexation is used for in situ product removal during enzymic kinetic cephalexin synthesis to prevent undesired hydrolysis. In order to achieve this, beneficial reaction conditions have to be matched with conditions that are beneficial for complexation. In the work described here, a pH of 7.5 and a temperature of 293 K meet these requirements best.The results were compared to predictions obtained with a model originally developed for cephalexin synthesis and which is now extended with complexation. For 1,5-dihydroxy-naphthalene, the course of the reaction was predicted accurately. For 2-naphthol, this was not the case; synthesis was enhanced and hydrolysis reduced compared to the model predictions for **immobilized** enzyme. On the other hand, the course of reactions could be predicted accurately by the model for liquid enzyme. Apparently, the reduced reaction rate (.apprx.30% residual activity) is such that mass transfer can keep up with it and diffusion limitation was lifted resulting in higher cephalexin concns.The effect of in situ complexation on productivity is discussed. It was found that complexation has a beneficial effect on overall cephalexin productivity and in most cases, hydrolysis is suppressed. The effects were most pronounced for liquid enzyme in combination with complexation with 1,5-dihydroxy-naphthalene for which, also exptl., the highest cephalexin concns. were measured.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 13 A + B ===> C...

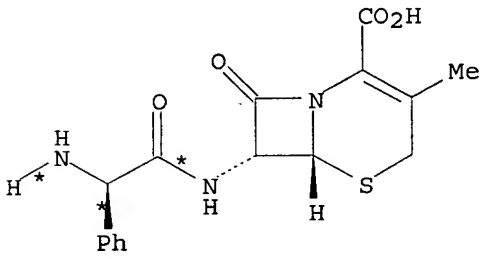


A



B

(1) →



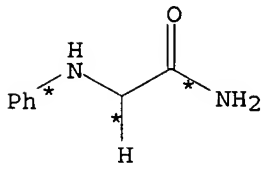
C

RX(1) RCT A 21969-70-0, B **22252-43-3**
RGT D 7647-01-0 HCl
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water

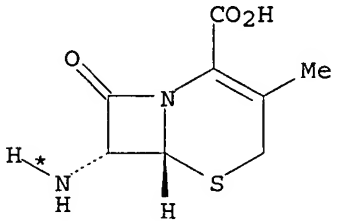
Searched by Barb O'Bryen, STIC 2-2518

NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

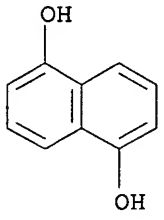
RX(2) OF 13 A + **B** + G ===> **H**



A

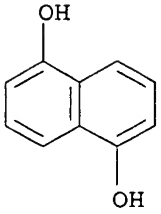


B

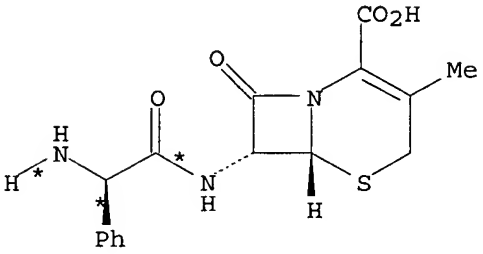


G

(2) →



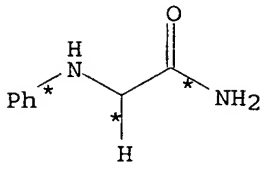
H: CM 1



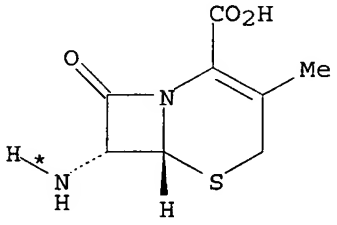
H: CM 2

RX(2) RCT A 21969-70-0, B **22252-43-3**, G 83-56-7
RGT D 7647-01-0 HCl
PRO H **473273-05-1**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

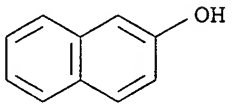
RX(3) OF 13 A + **B** + I ===> **J**



A

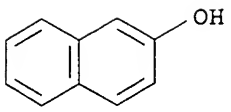


B

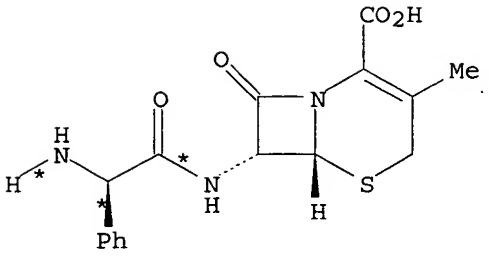


I

(3) →



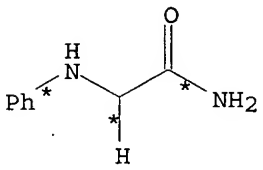
J: CM 1



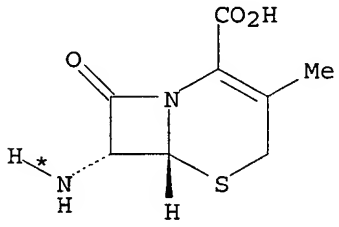
J: CM 2

RX(3) RCT A 21969-70-0, B **22252-43-3**, I 135-19-3
RGT D 7647-01-0 HCl
PRO J **61889-25-6**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

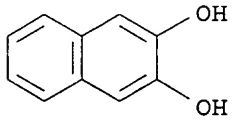
RX(4) OF 13 A + **B** + K ===> **L**



A

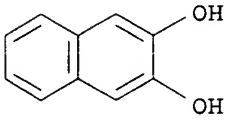


B

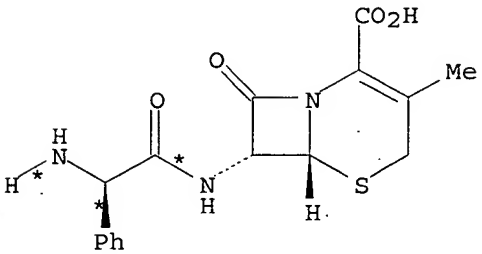


K

(4) ⟶



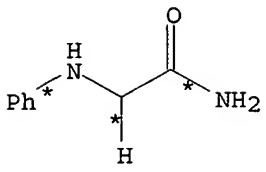
L: CM 1



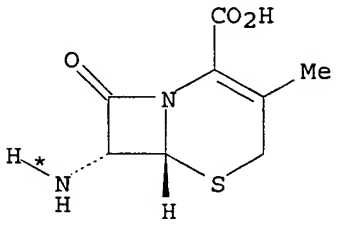
L: CM 2

RX(4) RCT A 21969-70-0, B **22252-43-3**, K 92-44-4
RGT D 7647-01-0 HCl
PRO L **473273-06-2**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

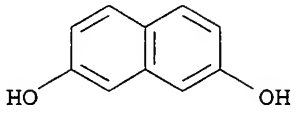
RX(5) OF 13 A + **B** + M ===> **N**



A

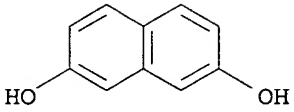


B

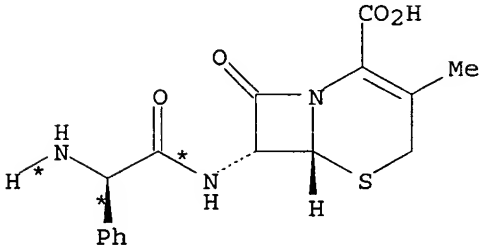


M

(5) →



N: CM 1

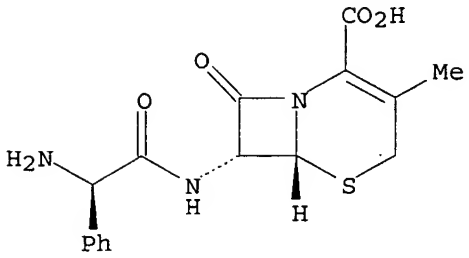


N: CM 2

RX(5) RCT A 21969-70-0, B **22252-43-3**, M 582-17-2
RGT D 7647-01-0 HCl
PRO N **473273-07-3**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

RX(6) OF 13 ...**C** + I ===> **J**

Searched by Barb O'Bryen, STIC 2-2518



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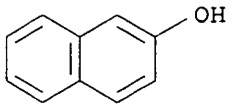
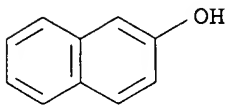
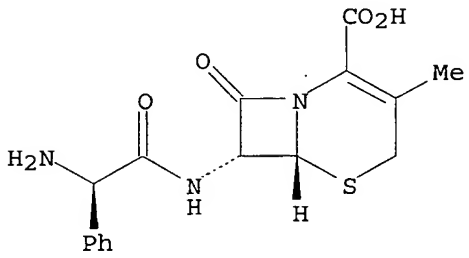


I

(6) →



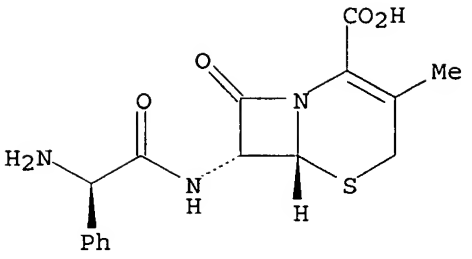
J: CM 1



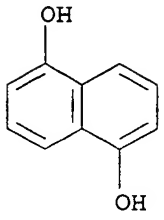
J: CM 2

RX(6) RCT C **15686-71-2**, I 135-19-3
RGT D 7647-01-0 HCl
PRO J **61889-25-6**
SOL 7732-18-5 Water
NTE buffered soln.

RX(7) OF 13 ...**C** + G ===> **H**

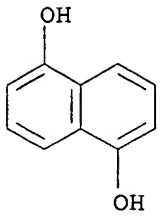


C

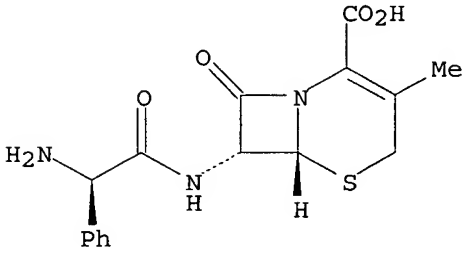


G

(7) →



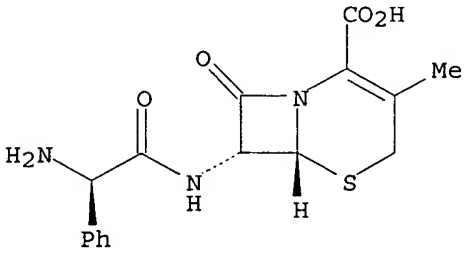
H: CM 1



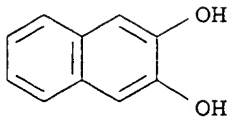
H: CM 2

RX(7) RCT C **15686-71-2**, G 83-56-7
RGT D 7647-01-0 HCl
PRO H **473273-05-1**
SOL 7732-18-5 Water
NTE buffered soln.

RX(8) OF 13 ...**C** + K ===> **L**

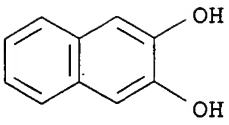


C

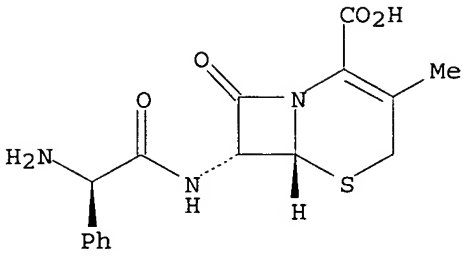


K

(8) →



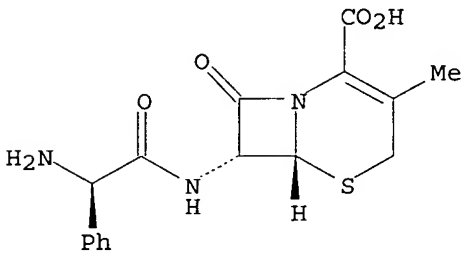
L: CM 1



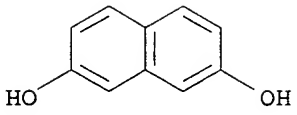
L: CM 2

RX(8) RCT C **15686-71-2**, K 92-44-4
RGT D 7647-01-0 HCl
PRO L **473273-06-2**
SOL 7732-18-5 Water
NTE buffered soln.

RX(9) OF 13 ...**C** + M ===> **N**

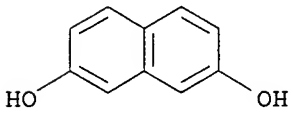


C

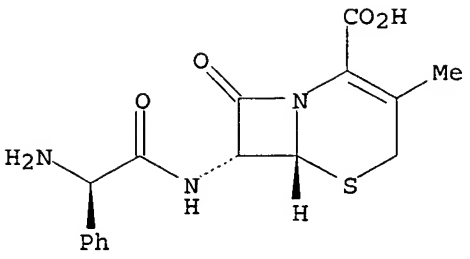


M

(9) ⟶



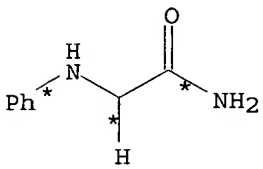
N: CM 1



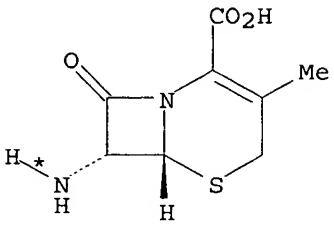
N: CM 2

RX(9) RCT C **15686-71-2**, M 582-17-2
RGT D 7647-01-0 HCl
PRO N **473273-07-3**
SOL 7732-18-5 Water
NTE buffered soln.

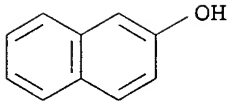
RX(10) OF 13 COMPOSED OF RX(1), RX(6)
RX(10) A + **B** + I ===> **J**



A

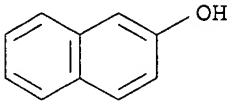


B

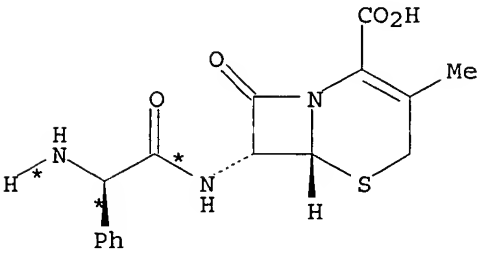


I

2
STEPS



J: CM 1

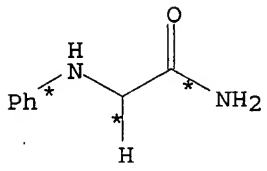


J: CM 2

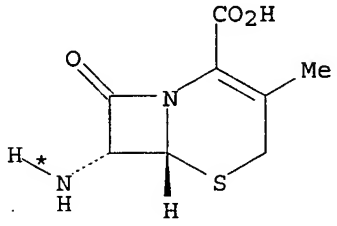
RX(1) RCT A 21969-70-0, B **22252-43-3**
RGT D 7647-01-0 HCl
PRO C 15686-71-2
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

RX(6) RCT C 15686-71-2, I 135-19-3
RGT D 7647-01-0 HCl
PRO J **61889-25-6**
SOL 7732-18-5 Water
NTE buffered soln.

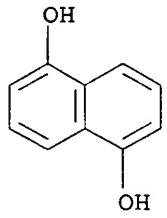
RX(11) OF 13 COMPOSED OF RX(1), RX(7)
RX(11) A + **B** + G ===> **H**



A

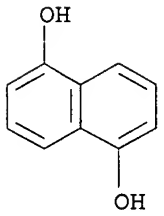


B

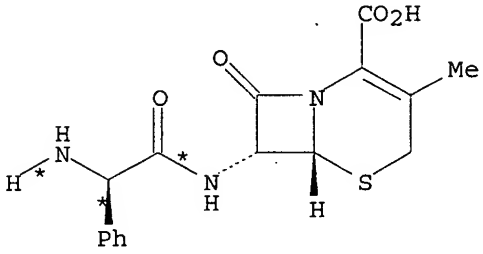


G

2 STEPS



H: CM 1

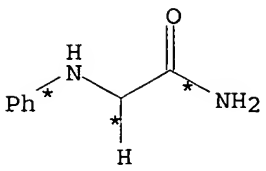


H: CM 2

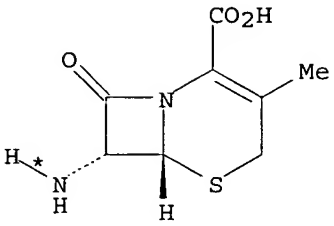
RX(1) RCT A 21969-70-0, B **22252-43-3**
RGT D 7647-01-0 HCl
PRO C 15686-71-2
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

RX(7) RCT C 15686-71-2, G 83-56-7
RGT D 7647-01-0 HCl
PRO H **473273-05-1**
SOL 7732-18-5 Water
NTE buffered soln.

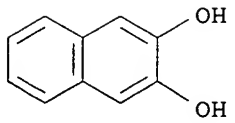
RX(12) OF 13 COMPOSED OF RX(1), RX(8)
RX(12) A + **B** + K ===> **L**



A

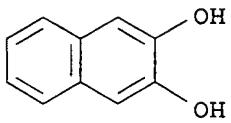


B

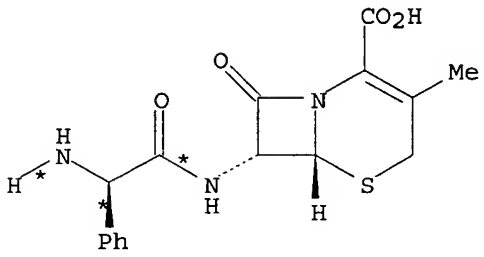


K

2
STEPS



L: CM 1

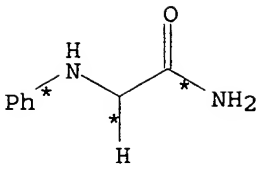


L: CM 2

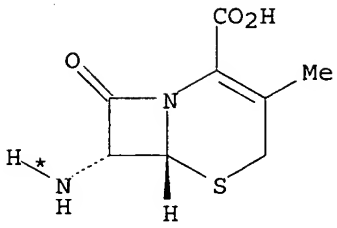
RX(1) RCT A 21969-70-0, B **22252-43-3**
RGT D 7647-01-0 HCl
PRO C 15686-71-2
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

RX(8) RCT C 15686-71-2, K 92-44-4
RGT D 7647-01-0 HCl
PRO L **473273-06-2**
SOL 7732-18-5 Water
NTE buffered soln.

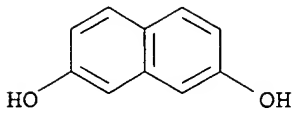
RX(13) OF 13 COMPOSED OF RX(1), RX(9)
RX(13) A + **B** + M ===> **N**



A

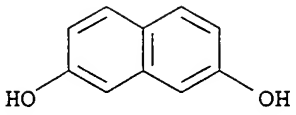


B

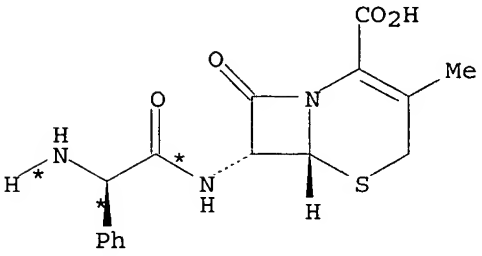


M

2 STEPS



N: CM 1



N: CM 2

RX(1) RCT A 21969-70-0, B **22252-43-3**
RGT D 7647-01-0 HCl
PRO C 15686-71-2
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE Escherichia coli ATCC 11105 immmobilized penicillin G acylase used, buffered soln., biotransformation, enzymic

RX(9) RCT C 15686-71-2, M 582-17-2
RGT D 7647-01-0 HCl
PRO N **473273-07-3**
SOL 7732-18-5 Water
NTE buffered soln.

AB In this paper, 'complexation' indicates the formation of clathrate type inclusion compds. of cephalexin with naphthalene derivs. These inclusion compds. readily crystallize in solution, resulting in specific co-crystals of complexing agent and cephalexin with a set ratio between both components. Complexation is used for in situ product removal during enzymic kinetic cephalexin synthesis to prevent undesired hydrolysis. In order to achieve this, beneficial reaction conditions have to be matched with conditions that are beneficial for complexation. In the work described here, a pH of 7.5 and a temperature of 293 K meet these requirements best.The results were compared to predictions obtained with a model originally developed for

cephalexin synthesis and which is now extended with complexation. For 1,5-dihydroxy-naphthalene, the course of the reaction was predicted accurately. For 2-naphthol, this was not the case; synthesis was enhanced and hydrolysis reduced compared to the model predictions for **immobilized** enzyme. On the other hand, the course of reactions could be predicted accurately by the model for liquid enzyme. Apparently, the reduced reaction rate (.apprx.30% residual activity) is such that mass transfer can keep up with it and diffusion limitation was lifted resulting in higher cephalexin concns.The effect of in situ complexation on productivity is discussed. It was found that complexation has a beneficial effect on overall cephalexin productivity and in most cases, hydrolysis is suppressed. The effects were most pronounced for liquid enzyme in combination with complexation with 1,5-dihydroxy-naphthalene for which, also exptl., the highest cephalexin concns. were measured.

IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**immobilized**; in situ product removal during enzymic cephalexin synthesis by complexation)

IT 9014-06-6, Penicillin Gacylase
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**immobilized**; in situ product removal during enzymic cephalexin synthesis by complexation)

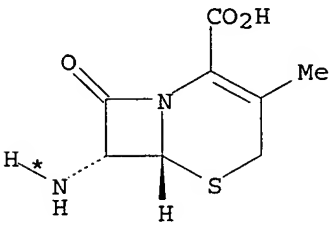
L37 ANSWER 13 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:68754 CASREACT
TITLE: Partitioning behaviour of cephalexin and 7-aminodeacetoxycephalosporanic acid in PEG/ammonium sulfate aqueous two-phase systems
AUTHOR(S): Zhu, Jian-Hang; Wei, Dong-Zhi; Cao, Xue-Jun; Liu, Ye-Qing; Yuan, Zhong-Yi
CORPORATE SOURCE: State Key Laboratory of Bioreactor Engineering, Institute of Biochemistry, East China University of Science and Technology, Shanghai, 200237, Peop. Rep. China
SOURCE: Journal of Chemical Technology & Biotechnology (2001), 76(11), 1194-1200
CODEN: JCTBED; ISSN: 0268-2575
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to develop an aqueous two-phase system (ATPS) for cephalexin synthesis with extractive bioconversion, the partitioning behavior of cephalexin and 7-aminodeacetoxycephalosporanic acid (7-ADCA) in poly(ethylene glycol) (PEG)/salt ATPS were examined Parameters such as PEG size, salt type and tie line length were investigated to find a primary extraction system. In PEG400/ammonium sulfate and PEG400/magnesium sulfate systems, the partition coefficient of cephalexin (KC) was larger than 1 while that of 7-ADCA (KA) deviated about 1.5. Addition of neutral salts, surfactants and water-miscible solvents were also investigated in the primary ATPS in order to improve the separation efficiency. KC greatly increased when neutral salts and surfactants were added to the PEG400/ammonium sulfate primary systems whereas KA was only slightly higher than that of the additive-free ATPS. In an improved ATPS for extractive bioconversion, consisting of PEG400 (20% weight/weight), ammonium sulfate (17.5% weight/weight), methanol (5% weight/weight) and NaCl (3% weight/weight), a KC value of up to 15.2 was achieved; KA was 1.8; KP (partition coefficient of

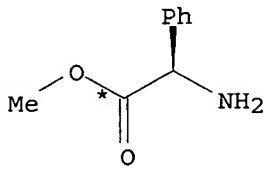
phenylglycine Me ester) was 1.2 and the recovery yield of cephalexin was 94.2%. The results obtained from the extractive bioconversion of cephalexin in the improved ATPS showed that it is feasible to perform such an enzymic process in an ATPS and the system offers the potential as a model for enzymic synthesis of some water soluble products.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 **A** + B ===> **C**



A



B

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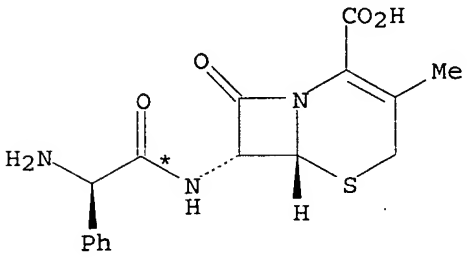


C

RX(1) RCT A **22252-43-3**, B 24461-61-8
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
NTE stereoselective, buffered soln., biotransformation, described medium, **immobilized** penicillin G acylase used, enzymic, alternatively aqueous two-phase system used

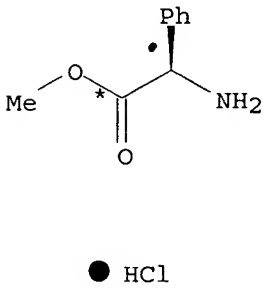
IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**immobilized**; partitioning behavior of cephalexin and 7-aminodeacetoxycephalosporanic acid in PEG/ammonium sulfate aqueous two-phase systems)

L37 ANSWER 14 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 136:81799 CASREACT
TITLE: Semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase
AUTHOR(S): Zhan, Xuanzhi; Yang, Sheng; Wang, Zheng; Zhu, Zhenqin; Yang, Lei; Yuan, Zhongyi
CORPORATE SOURCE: Shanghai Institute of Biochemistry, Academia Sinica,

Shanghai, 200031, Peop. Rep. China
SOURCE: Yaowu Shengwu Jishu (2001), 8(4), 192-196
CODEN: YSJIFO; ISSN: 1005-8915
PUBLISHER: Yaowu Shengwu Jishu Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

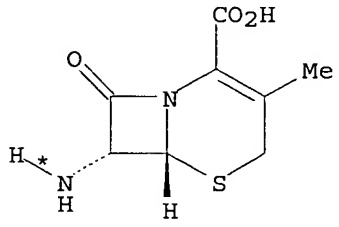
AB Semi-synthesis of cephalexin for 7-amino-3-deacetoxy-cephalosporanic acid (7-ADCA) and D-(-)-phenylglycine Me ester (PGME) using polyacrylonitrile (PAN) **immobilized** penicillin G acylase in the DMSO-water cosolvent was studied. The results were obtained as follows: (1) synthesis yield was markedly increased in comparing with that in the aqueous medium; **immobilized** enzyme maintained higher percentage of catalytic activity in aqueous organic cosolvent; (3) high concentration of substrate could be used. The cosolvent system, DMSO-water media was established on the basis of selection from difficult polar solvent. Effects of different conditions, such as solvent content, substrate concentration, pH, temperature on synthesis of cephalexin were analyzed. Under the optimal conditions: IPGA in 40% DMSO aqueous medium, 85 mmol/L 7-ADCA and 128 mmol/L PGME at pH 6.5, 25°. the conversion rate of 7-ADCA into cephalexin was >90% in 15 batches of semi-synthesis.

RX(1) OF 1 A + **B** ===> **C**



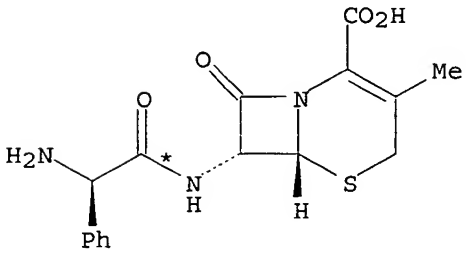
● HCl

A



B

(1) →



C

RX(1) RCT A 19883-41-1, B **22252-43-3**
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 67-68-5 DMSO, 7732-18-5 Water

NTE biotransformation, enzymic, at pH 6.5 and 25°, >90% conversion

TI Semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase

AB Semi-synthesis of cephalexin for 7-amino-3-deacetoxy-cephalosporanic acid (7-ADCA) and D-(-)-phenylglycine Me ester (PGME) using polyacrylonitrile (PAN) **immobilized** penicillin G acylase in the DMSO-water cosolvent was studied. The results were obtained as follows: (1) synthesis yield was markedly increased in comparing with that in the aqueous medium; **immobilized** enzyme maintained higher percentage of catalytic activity in aqueous organic cosolvent; (3) high concentration of substrate could be used. The cosolvent system, DMSO-water media was established on the basis of selection from difficult polar solvent. Effects of different conditions, such as solvent content, substrate concentration, pH, temperature on synthesis of cephalexin were analyzed. Under the optimal conditions: IPGA in 40% DMSO aqueous medium, 85 mmol/L 7-ADCA and 128 mmol/L PGME at pH 6.5, 25°. the conversion rate of 7-ADCA into cephalexin was >90% in 15 batches of semi-synthesis.

IT Temperature effects, biological
(semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase)

IT 9014-06-6
RL: CAT (Catalyst use); USES (Uses)
(**immobilized**; semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase)

IT 12408-02-5, Hydrogen ion, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase)

IT 57-55-6, Propylene glycol, uses 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-68-5, DMSO, uses 68-12-2, DMF, uses 107-21-1, Ethylene glycol, uses 109-99-9, THF, uses 7732-18-5, Water, uses
RL: NUU (Other use, unclassified); USES (Uses)
(semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase)

IT 19883-41-1, D-Phenylglycine methyl ester hydrochloride 22252-43-3, 7-ADCA
RL: RCT (Reactant); RACT (Reactant or reagent)
(semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase)

IT 15686-71-2P, Cephalexin
RL: SPN (Synthetic preparation); PREP (Preparation)
(semi-synthesis of cephalexin in DMSO-water medium by **immobilized** penicillin G acylase)

L37 ANSWER 15 OF 33 CASREACT COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 136:133642 CASREACT

TITLE: Cephalexin synthesis by **immobilised** penicillin G acylase under non-isothermal conditions: reduction of diffusion limitation

AUTHOR(S): Schroen, C. G. P. H.; Mohy Eldin, M. S.; Janssen, A. E. M.; Mita, G. D.; Tramper, J.

CORPORATE SOURCE: Food and Bioprocess Engineering Group, Wageningen University, Wageningen, 6700 EV, Neth.

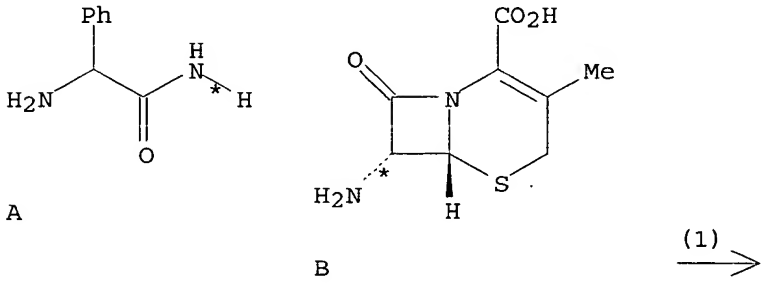
SOURCE: Journal of Molecular Catalysis B: Enzymatic (2001), 15(4-6), 163-172
CODEN: JMCEF8; ISSN: 1381-1177

PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of thermodialysis on the enzymic kinetic synthesis of the antibiotic cephalexin was investigated. As reference points, two existing models for an **immobilized** enzyme (Assemblase) and for the free enzyme were used. For Assemblase, it is known that diffusion limitation occurs and that therefore considerably more of the undesired side-product phenylglycine is formed.The enzyme was **immobilized** on a membrane, and under isothermal conditions (293 K) the course of the reaction resembled that of the Assemblase enzyme. However, if a temperature gradient was applied across the membrane, with an average temperature of 293 K for the enzyme, than the course of the reaction changed. For large temperature gradients (30° and more), the course of the reaction resembled that of free enzyme. Thermodialysis enhances mass transfer across the membrane and therewith reduces diffusion limitations in the **immobilized** enzyme on the membrane.The stability of the **immobilized** enzyme is such that the reactor can be re-used repeatedly. This, together with the pos. effect of the temperature gradient on the course of the reaction, makes thermodialysis an interesting new technique that has potential to be applied on a larger scale if the membrane surface area per volume of reactor can be improved.

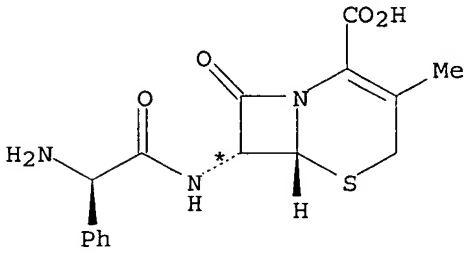
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 A + **B** ===> **C**



A

B



C

RX(1) RCT A 700-63-0, B **22252-43-3**
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase

Searched by Barb O'Bryen, STIC 2-2518

SOL 7732-18-5 Water
NTE enzymic, biotransformation, Assemblase enzyme **immobilised** on memrane used, stereoselective, alternative reaction conditions shown

TI Cephalexin synthesis by **immobilised** penicillin G acylase under non-isothermal conditions: reduction of diffusion limitation

AB The effect of thermodialysis on the enzymic kinetic synthesis of the antibiotic cephalexin was investigated. As reference points, two existing models for an **immobilized** enzyme (Assemblase) and for the free enzyme were used. For Assemblase, it is known that diffusion limitation occurs and that therefore considerably more of the undesired side-product phenylglycine is formed.The enzyme was **immobilized** on a membrane, and under isothermal conditions (293 K) the course of the reaction resembled that of the Assemblase enzyme. However, if a temperature gradient was applied across the membrane, with an average temperature of 293 K for the enzyme, than the course of the reaction changed. For large temperature gradients (30° and more), the course of the reaction resembled that of free enzyme. Thermodialysis enhances mass transfer across the membrane and therewith reduces diffusion limitations in the **immobilized** enzyme on the membrane.The stability of the **immobilized** enzyme is such that the reactor can be re-used repeatedly. This, together with the pos. effect of the temperature gradient on the course of the reaction, makes thermodialysis an interesting new technique that has potential to be applied on a larger scale if the membrane surface area per volume of reactor can be improved.

ST **immobilized** penicillin acylase cephalexin synthesis

IT Reaction kinetics
(biochem.; reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

IT **Immobilization**, molecular or cellular
(enzyme; reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

IT Mass transfer
(interfacial; reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

IT Bioreactors
(membrane; reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

IT Dialysis
Diffusion
Enzyme kinetics
(reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

IT 9014-06-6
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

IT 700-63-0 22252-43-3, 7-Aminodeacetoxycephalosporanic acid
RL: BCP (Biochemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(reduction of diffusion limitation during cephalexin synthesis by

immobilized penicillin G acylase under non-isothermal conditions)

IT 15686-71-2P, Cephalexin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

IT 2835-06-5P
RL: BYP (Byproduct); PREP (Preparation)
(reduction of diffusion limitation during cephalexin synthesis by **immobilized** penicillin G acylase under non-isothermal conditions)

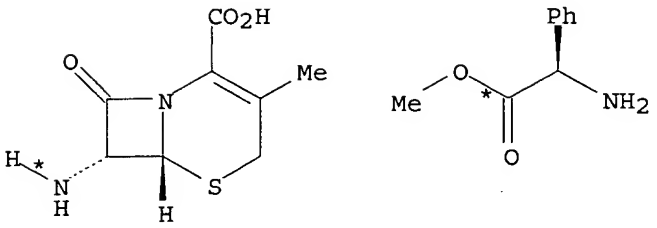
L37 ANSWER 16 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 141:259470 CASREACT
TITLE: An enzymatic process for the manufacture of semisynthetic β-lactam antibiotics
INVENTOR(S): Mali, Subhas; Gupte, Rajan; Deshpande, Jayant
PATENT ASSIGNEE(S): Kopran Ltd., India
SOURCE: Indian, 11 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 185088	A	20001111	IN 1998-BO475	19980722

PRIORITY APPLN. INFO.: IN 1998-BO475 19980722
OTHER SOURCE(S): MARPAT 141:259470

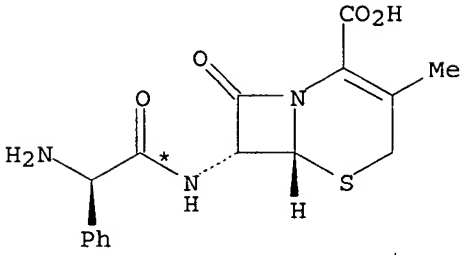
AB The invention relates to an enzymic process for the preparation of semisynthetic antibiotic in which the β-lactam nucleus is acylated with large excess of a side chain acylating agent ester. The excess, unreacted acylating agent is then recovered from reaction mass by extraction with an organic solvent. More than 90% of the unreacted side chain ester is recovered with high purity (>99%). This make it possible to obtain a com. attractive process for the enzymic preparation of semisynthetic antibiotics. Thus, penicillin amidase was employed to biosynthesize cephalexin by acylation of 7-amino-desacetoxy-cephalosporanic acid with D-Ph glycine Me ester.

RX(1) OF 3 ...**A** + B ===> **C**



A ● HCl

B (1) ⟶



● H_2O

C

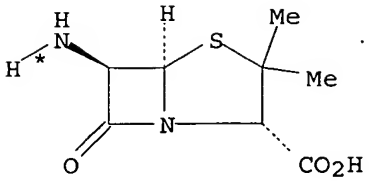
RX(1) RCT A **22252-43-3**, B 19883-41-1

STAGE(1)
RGT D 7664-41-7 NH3
CAT **9014-06-6** Penicillin amidase
SOL 75-09-2 CH2Cl2, 7732-18-5 Water
CON SUBSTAGE(1) room temperature, pH 6.5
SUBSTAGE(2) room temperature -> 10 deg C
SUBSTAGE(4) 60 minutes

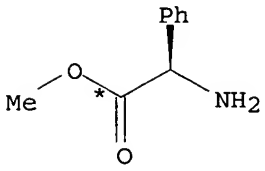
STAGE(2)
RGT E 7647-01-0 HCl
SOL 7732-18-5 Water
CON pH 6.1

PRO C **23325-78-2**
NTE biotransformation, enzymic, optimization study, **Immobilised** Penicillin G Amidase enzyme from E. coli was used

RX(2) OF 3 I + 2 J ===> B + K...



I



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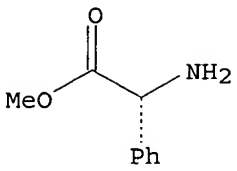
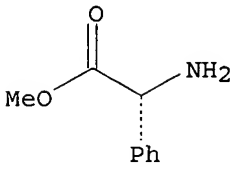
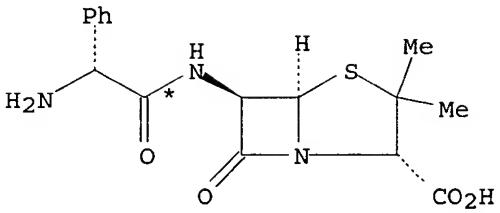


J

(2) →



B



K

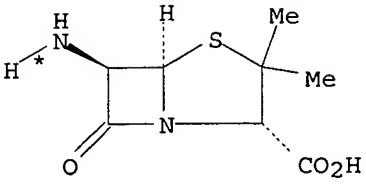
RX(2) RCT I 551-16-6, J 24461-61-8

STAGE(1)
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON SUBSTAGE(1) room temperature, pH 6.5
SUBSTAGE(2) room temperature
SUBSTAGE(3) 4 hours, 20 deg C

STAGE(2)
RGT E 7647-01-0 HCl
CON 45 minutes

PRO B 19883-41-1, K 69-53-4
NTE biotransformation, enzymic, **Immobilised** Penicillin G
Amidase enzyme from E. coli was used

RX(3) OF 3 COMPOSED OF RX(2), RX(1)
RX(3) I + 2 J + **A** ===> **C**



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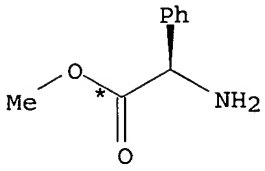
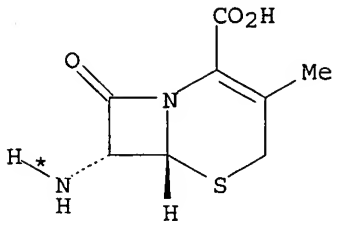
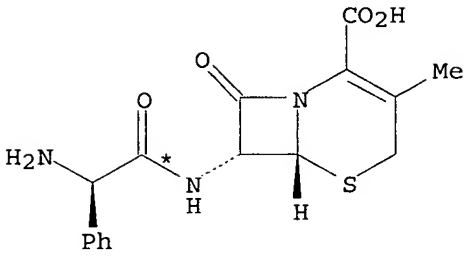


2 J



A

2
STEPS
→



● H_2O

C

RX(2) RCT I 551-16-6, J 24461-61-8

STAGE(1)
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water
CON SUBSTAGE(1) room temperature, pH 6.5
SUBSTAGE(2) room temperature
SUBSTAGE(3) 4 hours, 20 deg C

STAGE(2)
RGT E 7647-01-0 HCl
CON 45 minutes

PRO B 19883-41-1, K 69-53-4
NTE biotransformation, enzymic, **Immobilised** Penicillin G Amidase enzyme from E. coli was used

RX(1) RCT A **22252-43-3**, B 19883-41-1

STAGE(1)
RGT D 7664-41-7 NH3
CAT **9014-06-6** Penicillin amidase

Searched by Barb O'Bryen, STIC 2-2518

SOL 75-09-2 CH2Cl2, 7732-18-5 Water
CON SUBSTAGE(1) room temperature, pH 6.5
SUBSTAGE(2) room temperature -> 10 deg C
SUBSTAGE(4) 60 minutes

STAGE(2)
RGT E 7647-01-0 HCl
SOL 7732-18-5 Water
CON pH 6.1

PRO C **23325-78-2**
NTE biotransformation, enzymic, optimization study, **Immobilised** Penicillin G Amidase enzyme from E. coli was used

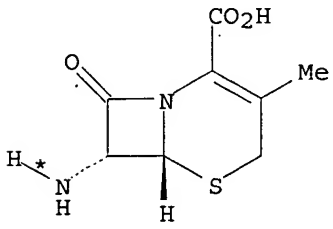
IT Enzymes, uses
RL: BCP (Biochemical process); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(**immobilized**; enzymic process for manufacture of semisynthetic β-lactam antibiotics)

L37 ANSWER 17 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 129:67616 CASREACT
TITLE: Use of aqueous two-phase systems for in situ extraction of water soluble antibiotics during their synthesis by enzymes **immobilized** on porous supports
AUTHOR(S): Hernandez-Justiz, Odette; Fernandez-Lafuente, Roberto; Terreni, Marco; Guisan, Jose M.
CORPORATE SOURCE: Laboratorio de Tecnologia Enzimatica, Universidad Autonoma, Madrid, 28049, Spain
SOURCE: Biotechnology and Bioengineering (1998), 59(1), 73-79
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

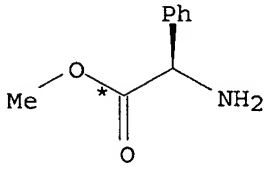
AB Yields of kinetically controlled synthesis of antibiotics catalyzed by penicillin G acylase from Escherichia coli (PGA) have been greatly increased by continuous extraction of water soluble products (cephalexin) away from the surroundings of the enzyme. In this way its very rapid enzymic hydrolysis has been avoided. Enzymes covalently **immobilized** inside porous supports acting in aqueous two-phase systems have been used to achieve such improvements of synthetic yields. Before the reaction is started, the porous structure of the bio-catalyst can be washed and filled with one selected phase. In this way, when the pre-equilibrated biocatalyst is mixed with the second phase where the reaction product will be extracted the **immobilized** enzyme remains in the first selected phase in spite of its possibly different natural trend. Partition coeffs. (K) of cephalexin in very different aqueous two-phase systems were firstly evaluated. High K values were obtained under drastic conditions. The best K value for cephalexin (23) was found in 100% PEG 600-3 M ammonium sulfate where cephalexin was extracted to the PEG phase. Pre-incubation of **immobilized** PGA derivs. in ammonium sulfate and further suspension with 100% PEG 600 allowed us to obtain a 90% synthetic yield of cephalexin from 150 mM phenylglycine Me ester and 100 mM 7-amino desacetoxicephalosporanic acid (7-ADCA). In this reaction system, the i.m.-mobilized enzyme remains in the ammonium sulfate phase and hydrolysis of the antibiotic becomes suppressed because of its continuous extraction to the PEG phase. On the contrary, synthetic yields of a similar process carried out in monophasic systems were much lower (55%) because of a rapid

enzymic hydrolysis of cephalexin.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

RX(1) OF 1 **A** + B ===> **C**



A



B

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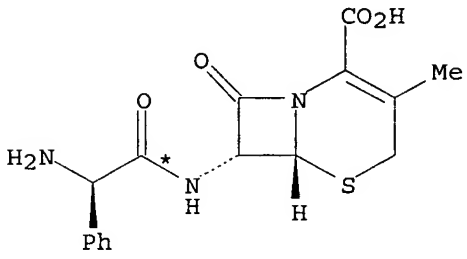


C

RX(1) RCT A **22252-43-3**, B 24461-61-8
PRO C **15686-71-2**
CAT **9014-06-6** Penicillin amidase
SOL 7732-18-5 Water, 25322-68-3 HOCH2CH2OH polymer

TI Use of aqueous two-phase systems for in situ extraction of water soluble antibiotics during their synthesis by enzymes **immobilized** on porous supports

AB Yields of kinetically controlled synthesis of antibiotics catalyzed by penicillin G acylase from Escherichia coli (PGA) have been greatly increased by continuous extraction of water soluble products (cephalexin) away from the surroundings of the enzyme. In this way its very rapid enzymic hydrolysis has been avoided. Enzymes covalently **immobilized** inside porous supports acting in aqueous two-phase systems have been used to achieve such improvements of synthetic yields. Before the reaction is started, the porous structure of the bio-catalyst can be washed and filled with one selected phase. In this way, when the pre-equilibrated biocatalyst is mixed with the second phase where the reaction product will be extracted the **immobilized** enzyme remains in the first selected phase in spite of its possibly different natural trend. Partition coeffs. (K) of cephalexin in very different aqueous two-phase systems were firstly evaluated. High K values were obtained under drastic conditions. The best K value for cephalexin (23) was found in 100% PEG 600-3 M ammonium sulfate where cephalexin was extracted to the PEG phase. Pre-incubation of **immobilized** PGA derivs. in ammonium sulfate and further suspension with 100% PEG 600 allowed us to obtain a 90% synthetic yield of cephalexin from 150 mM phenylglycine Me ester and 100 mM 7-amino

desacetoxicephalosporanic acid (7-ADCA). In this reaction system, the i.m.-mobilized enzyme remains in the ammonium sulfate phase and hydrolysis of the antibiotic becomes suppressed because of its continuous extraction to the PEG phase. On the contrary, synthetic yields of a similar process carried out in monophasic systems were much lower (55%) because of a rapid enzymic hydrolysis of cephalexin.

ST cephalexin synthesis enzymic kinetically controlled; **immobilized** catalyst porous support; aq biphase system cephalexin synthesis

IT Organic synthesis
(enzymic kinetically controlled; use of aqueous two-phase systems for in situ extraction of water soluble antibiotics during their synthesis by enzymes **immobilized** on porous supports)

IT Lactams
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(β-; use of aqueous two-phase systems for in situ extraction of water soluble antibiotics during their synthesis by enzymes **immobilized** on porous supports)

IT 15686-71-2P, Cephalexin
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(use of aqueous two-phase systems for in situ extraction of water soluble antibiotics during their synthesis by enzymes **immobilized** on porous supports)

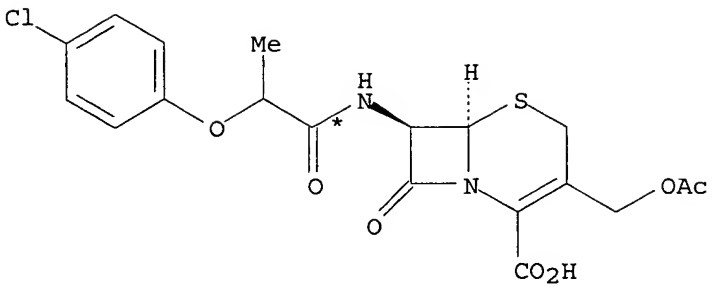
IT 9014-06-6
RL: BPR (Biological process); BSU (Biological study, unclassified); CAT (Catalyst use); BIOL (Biological study); PROC (Process); USES (Uses)
(use of aqueous two-phase systems for in situ extraction of water soluble antibiotics during their synthesis by enzymes **immobilized** on porous supports)

IT 22252-43-3, 7-Amino desacetoxycephalosporanic acid 24461-61-8, (D)-Phenylglycine methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(use of aqueous two-phase systems for in situ extraction of water soluble antibiotics during their synthesis by enzymes **immobilized** on porous supports)

L37 ANSWER 18 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 120:216301 CASREACT
TITLE: Enantioselective hydrolysis of 2-aryloxypropionyl derivatives by penicillin V amidase
AUTHOR(S): Chen, S. T.; Chang, C. M.; Lin, S. L.; Wang, K. T.
CORPORATE SOURCE: Inst. Biol. Chem., Acad. Sin., Taipei, 10098, Taiwan
SOURCE: Journal of the Chinese Chemical Society (Taipei, Taiwan) (1993), 40(5), 489-91
CODEN: JCCTAC; ISSN: 0009-4536
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Selective hydrolysis of 2-aryloxypropionyl derivs. and 2-phenoxybutyrate catalyzed by an **immobilized** penicillin V amidase, Semacylase, showed moderate to low enantiomeric excess.

RX(1) OF 3 ...A ===> B



A

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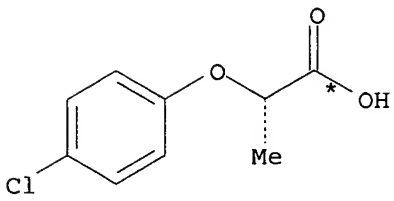
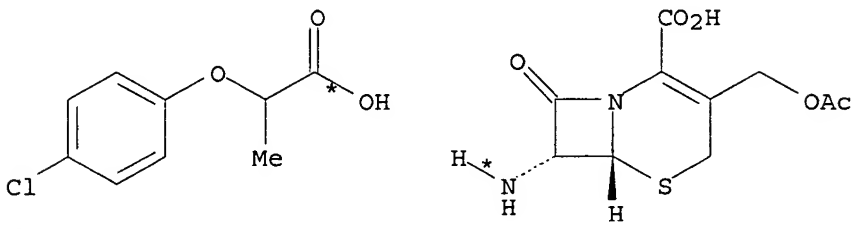


B
YIELD 76%

RX(1) RCT A 153907-70-1
PRO B 20421-35-6
CAT **9014-06-6** Penicillin amidase
SOL 68-12-2 DMF, 7732-18-5 Water
NTE phosphate buffer

RX(2) OF 3 F + G ===> A...

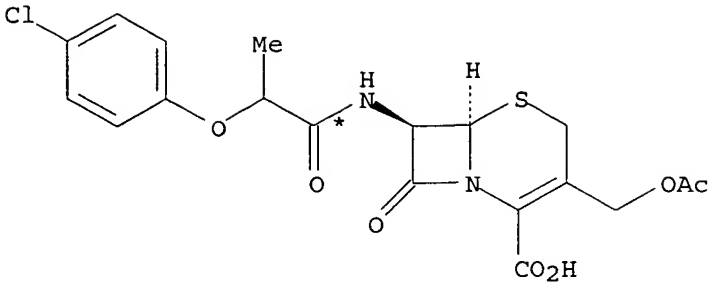


F

● HCl

G

(2) →



A
YIELD 85%

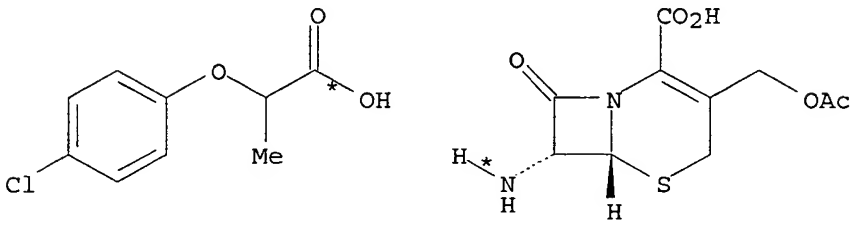
RX(2) RCT F 3307-39-9.

STAGE(1)
RGT H 538-75-0 DCC, I 6066-82-6 N-Hydroxysuccinimide
SOL 68-12-2 DMF, 141-78-6 AcOEt

STAGE(2)
RCT G **57399-61-8**
RGT J 121-44-8 Et3N
SOL 68-12-2 DMF

PRO A **153907-70-1**

RX(3) OF 3 COMPOSED OF RX(2), RX(1)
RX(3) F + G ===> B

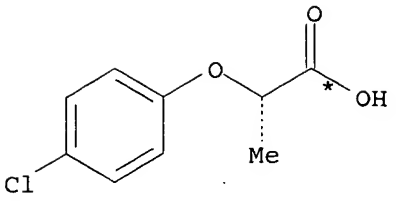


F

● HCl

G

2
STEPS
⟶



B
YIELD 76%

RX(2) RCT F 3307-39-9

STAGE(1)
RGT H 538-75-0 DCC, I 6066-82-6 N-Hydroxysuccinimide
SOL 68-12-2 DMF, 141-78-6 AcOEt

STAGE(2)
RCT G 57399-61-8
RGT J 121-44-8 Et3N
SOL 68-12-2 DMF

PRO A 153907-70-1

RX(1) RCT A 153907-70-1
PRO B 20421-35-6
CAT **9014-06-6** Penicillin amidase
SOL 68-12-2 DMF, 7732-18-5 Water
NTE phosphate buffer

AB Selective hydrolysis of 2-aryloxypropionyl derivs. and 2-phenoxybutyrate catalyzed by an **immobilized** penicillin V amidase, Semacylase, showed moderate to low enantiomeric excess.

L37 ANSWER 19 OF 33 CASREACT COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 83:112370 CASREACT
TITLE: Enzymic synthesis of semisynthetic penicillins and cephalosporins using an insoluble acylase
INVENTOR(S): Bartoli, Francesco; Cecere, Francesco; Galli, Giuliano
PATENT ASSIGNEE(S): Snamprogetti SpA, Italy
SOURCE: Ger. Offen., 9 pp. Addn. to. Ger. Offen. 1,932,426.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2460649	A1	19750626	DE 1974-2460649	19741220
AU 7475938	A1	19760603	AU 1974-75938	19741202
FR 2255379	A1	19750718	FR 1974-39837	19741205
CH 606432	A	19781031	CH 1974-16401	19741210
ZA 7407896	A	19751231	ZA 1974-7896	19741211
BE 823393	A1	19750416	BE 1974-151539	19741216
FI 7403621	A	19750621	FI 1974-3621	19741216
GB 1482481	A	19770810	GB 1974-54337	19741216

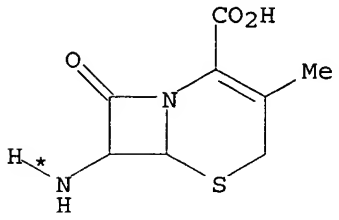
Searched by Barb O'Bryen, STIC 2-2518

NL 7416548	A	19750624	NL 1974-16548	19741218
DK 7406610	A	19750825	DK 1974-6610	19741218
NO 7404591	A	19750623	NO 1974-4591	19741219
SE 7416078	A	19750623	SE 1974-16078	19741219
HU 172712	P	19781128	HU 1974-SA2732	19741219
JP 50095487	A2	19750729	JP 1974-145851	19741220
DD 115683	C	19751012	DD 1974-183278	19741220
CS 190459	P	19790531	CS 1974-8820	19741220

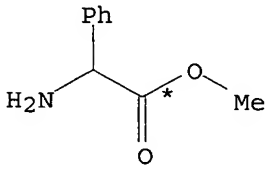
PRIORITY APPLN. INFO.: IT 1973-54486 19731220

AB 7β-Aminophenylacetamido)-3-methylceph-3-em-4-carboxylic acid (cephalexin) [15686-71-2] was prepared by the reaction of 7-amino-3-methylceph-3-em-4-carboxylic acid (7-ADCA) [22252-43-3] and D(-)-phenylglycine methyl ester-chlorohydrate (PGM) [19883-41-1] in contact with a pulp of cellulose triacetate (CTA) containing penicillinacylase [9014-06-6]. In a like manner, 6-aminopenicillinic acid (6-APA) [551-16-6] and D(-)-p-hydroxyphenylglycine ethyl ester (p-OH PGE) [43189-38-4] in contact with the enzyme-containing pulp yielded α-amino-p-hydroxybenzylpenicillin (amoxicillin) [26787-78-0]. The enzyme was extracted from Escherichia coli strain ATCC 9637.

RX(1) OF 1 **A** + B ===> **C**

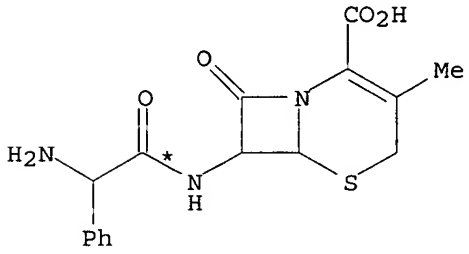


A



B

(1) →



C

YIELD 73%

RX(1) RCT A **26395-99-3**, B 26682-99-5
PRO C **108260-04-4**
CAT **9014-06-6** Penicillin amidase
NTE Biotransformation: catalyzed by penicillin amidase from escherichia coli; # Conditions: 500 mg educt + 1 g methyl d-(-)-phenylglycinate chlorohydrate; 2 g cellfree enzyme **immobilized** with cellulose triacetate (2500 u/g); 50 ml p-buffer ph 7,0; 1 h, 25.deg.c

IT 551-16-6 43189-38-4
RL: BIOL (Biological study)
(amoxicillin manufacture from, with **immobilized** acylase)
IT 9014-06-6
RL: PROC (Process)
(**immobilization** of, on cellulose triacetate, in synthetic penicillin manufacture)
IT 15686-71-2P 26787-78-0P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with **immobilized** acylase)

L37 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:79264 CAPLUS
DOCUMENT NUMBER: 144:145424
TITLE: Immobilization of microbial penicillin-G-acylase on derivatized hydrophobic epoxide **resin** for the production of β-lactam antibiotics
INVENTOR(S): Terreni, Marco; Vaccaro, Susanna; Estruch, Ilona; Pregnolato, Massimo; Giannelli, Antonio; Caruso, Salvatore
PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Innovate Biotechnology S.r.l.
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006008296	A1	20060126	WO 2005-EP53474	20050719

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

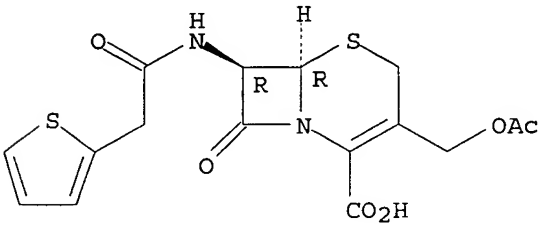
PRIORITY APPLN. INFO.: IT 2004-PD191 A 20040719
OTHER SOURCE(S): CASREACT 144:145424
ED Entered STN: 27 Jan 2006
AB Herein described is a process for the preparation of enzymic catalysts immobilized on solid hydrophobic epoxide support, particularly suitable for the synthesis of β-lactamic antibiotics; the enzymic catalysts obtainable by this process and their use. The process comprises partial oxidation of the surface epoxide groups into aldehyde groups; immobilization of an enzyme onto the surface of the derivatized epoxide support; hydrophilization of the surface of the support. More specifically, immobilization of penicillin-G-acylase from Escherichia coli on hydrophobic epoxidic resin (e.g., Eupergit C or Sepabeads EC-EP) is

described. Synthesis of cephazoline with E. coli penicillin-G-acylase immobilized on Eupergit C or Sepabeads EC-EP is also reported.

IT **153-61-7P**, Cephalotin **25953-19-9P**, Cephazoline
53994-73-3P, Cephaclor **92665-29-7P**, Cephprozyl
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(immobilization of microbial penicillin-G-acylase on derivatized hydrophobic epoxide **resin** for production of β-lactam antibiotics)

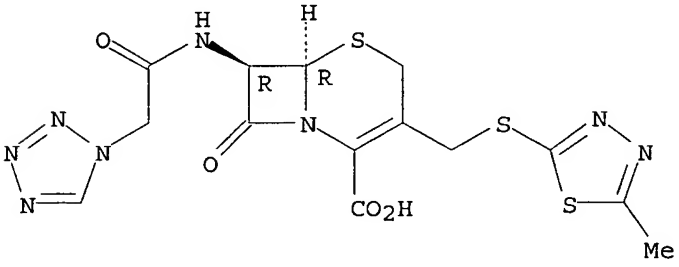
RN 153-61-7 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



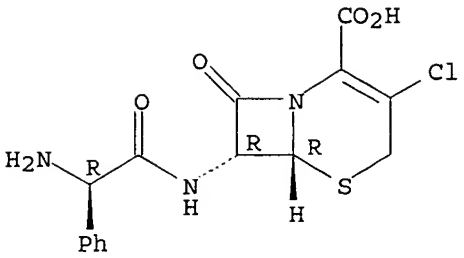
RN 25953-19-9 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[(5-methyl-1,3,4-thiadiazol-2-yl)thio]methyl]-8-oxo-7-[(1H-tetrazol-1-ylacetyl)amino]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



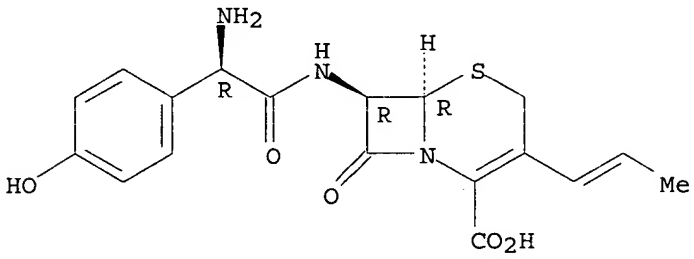
RN 53994-73-3 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-chloro-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



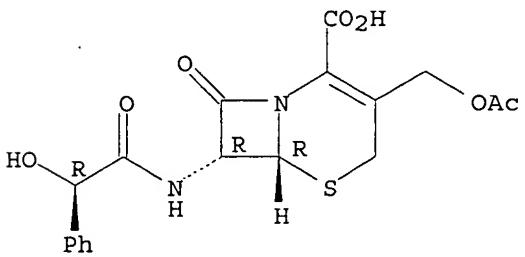
RN 92665-29-7 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-amino(4-hydroxyphenyl)acetyl]amino]-8-oxo-3-(1-propenyl)-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



IT **51818-85-0P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(immobilization of microbial penicillin-G-acylase on derivatized hydrophobic epoxide **resin** for production of β-lactam antibiotics)
RN 51818-85-0 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-7-[[(2R)-hydroxyphenylacetyl]amino]-8-oxo-, (6R,7R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9014-06-6DP**, Penicillin-G-acylase, immobilized derivs.
RL: CAT (Catalyst use); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(immobilization of microbial penicillin-G-acylase on derivatized hydrophobic epoxide **resin** for production of β-lactam

antibiotics)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

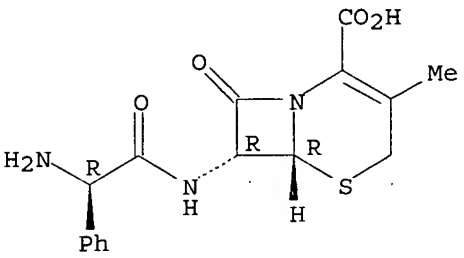
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:127150 CAPLUS
DOCUMENT NUMBER: 144:410853
TITLE: High-level production and covalent immobilization of Providencia rettgeri penicillin G acylase (PAC) from recombinant Pichia pastoris for the development of a novel and stable biocatalyst of industrial applicability
AUTHOR(S): Senerovic, Lidija; Stankovic, Nada; Spizzo, Patrizia; Basso, Alessandra; Gardossi, Lucia; Vasiljevic, Branka; Ljubljankic, Goran; Tisminetzky, Sergio; Degrassi, Giuliano
CORPORATE SOURCE: Institute of Molecular Genetics and Genetic Engineering, Belgrade,
SOURCE: Biotechnology and Bioengineering (2006), 93(2), 344-354
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 10 Feb 2006
AB A complete, integrated process for the production of an innovative formulation of penicillin G acylase from Providencia rettgeri (rPACP.rett) of industrial applicability is reported. In order to improve the yield of rPAC, the clone LN5.5, carrying four copies of pac gene integrated into the genome of Pichia pastoris, was constructed. The proteinase activity of the recombinant strain was reduced by knockout of the PEP4 gene encoding for proteinase A, resulting in an increased rPACP.rett activity of approx. 40% (3.8 U/mL vs. 2.7 U/mL produced by LN5.5 in flask). A high cell d. fermentation process was established with a 5-day methanol induction phase and a final PAC activity of up to 27 U/mL. A single step rPACP.rett purification was also developed with an enzyme activity yield of approx. 95%. The novel features of the rPACP.rett expressed in P.pastoris were fully exploited and emphasized through the covalent immobilization of rPACP.rett. The enzyme was immobilized on a series of structurally correlated **methacrylic** polymers, specifically designed and produced for optimizing rPACP.rett performances in both hydrolytic and synthetic processes. Polymers presenting aminic functionalities were the most efficient, leading to formulations with higher activity and stability (half time stability >3 years and specific activity ranging from 237 to 477 U/gdry based on benzylpenicilin hydrolysis). The efficiency of the immobilized rPACP.rett was finally evaluated by studying the kinetically controlled synthesis of β-lactam antibiotics (cephalexin) and estimating the synthesis/hydrolysis ratio (S/H), which is a crucial parameter for the feasibility of the process.
IT **9014-06-6P**, Penicillin G acylase
RL: BCP (Biochemical process); BMF (Bioindustrial manufacture); **CAT (Catalyst use)**; PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(production of Providencia rettgeri penicillin G acylase using recombinant Pichia pastoris, covalent immobilization and use in cepahalexin biosynthesis)

RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **15686-71-2P**, Cephalexin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(production of Providencia rettgeri penicillin G acylase using recombinant Pichia pastoris, covalent immobilization and use in cepahalexin biosynthesis)
RN 15686-71-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

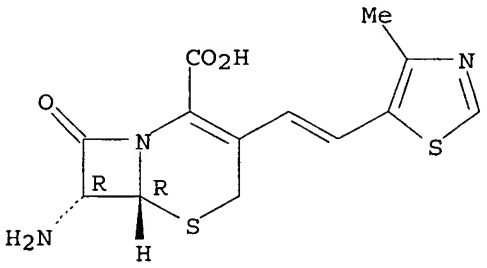
L37 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1310503 CAPLUS
DOCUMENT NUMBER: 144:51371
TITLE: Process for production of 3-alkenylcephem compounds
INVENTOR(S): Nishioka, Yoichi; Ito, Masahiro; Kameyama, Yutaka
PATENT ASSIGNEE(S): Otsuka Chemical Co., Ltd., Japan; Meiji Seika Kaisha Ltd.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005118595	A1	20051215	WO 2005-JP10621	20050603

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

JP 2005343854 A2 20051215 JP 2004-167581 20040604
PRIORITY APPLN. INFO.: JP 2004-167581 A 20040604
OTHER SOURCE(S): CASREACT 144:51371; MARPAT 144:51371
ED Entered STN: 16 Dec 2005
AB This document discloses a process for the production of 7-amino-3-[(E/Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid and alkali metal salts thereof which contain a large amount of 7-amino-3-[(Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid and alkali metal salts thereof, characterized by adding a high-porous polymer and/or activated carbon to an aqueous solution of an alkali metal salt of 7-amino-3-[(E/Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem -4-carboxylic acid. Thus, an aqueous solution of 7-amino-3-[(E/Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid sodium salt was treated with activated carbon and then with HCl to give 7-amino-3-[(E/Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid which contained 99.92% 7-amino-3-[(Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid.
IT **871117-63-4P 871117-64-5P**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(process for production and purification of 7-amino-3-[(Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid)
RN 871117-63-4 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-[2-(4-methyl-5-thiazolyl)ethenyl]-8-oxo-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

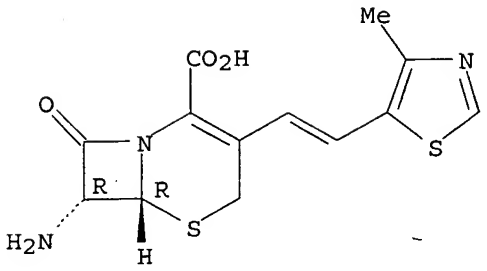
Absolute stereochemistry.
Double bond geometry unknown.



● Na

RN 871117-64-5 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-[2-(4-methyl-5-thiazolyl)ethenyl]-8-oxo-, monopotassium salt, (6R,7R)- (9CI) (CA INDEX NAME)

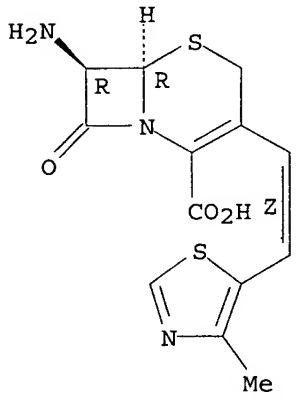
Absolute stereochemistry.
Double bond geometry unknown.



● K

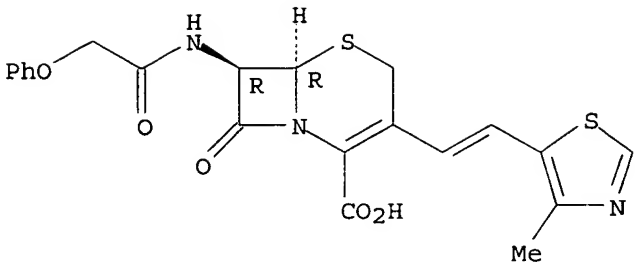
IT **155723-02-7P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(process for production and purification of 7-amino-3-[(Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid)
RN 155723-02-7 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-[(1Z)-2-(4-methyl-5-thiazolyl)ethenyl]-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **104145-83-7P 871117-67-8P 871117-68-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for production and purification of 7-amino-3-[(Z)-2-(4-methylthiazol-5-yl)vinyl]-3-cephem-4-carboxylic acid)
RN 104145-83-7 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[2-(4-methyl-5-thiazolyl)ethenyl]-8-oxo-7-[(phenoxyacetyl)amino]-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

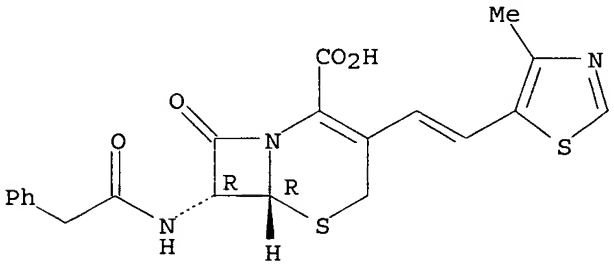
Absolute stereochemistry.
Double bond geometry unknown.



● Na

RN 871117-67-8 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[2-(4-methyl-5-thiazolyl)ethenyl]-8-oxo-7-[(phenylacetyl)amino]-, monosodium salt, (6R,7R)- (9CI) (CA INDEX NAME)

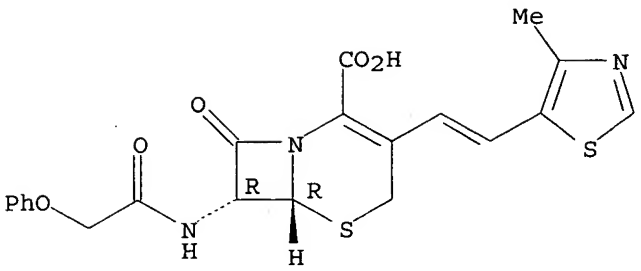
Absolute stereochemistry.
Double bond geometry unknown.



● Na

RN 871117-68-9 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[2-(4-methyl-5-thiazolyl)ethenyl]-8-oxo-7-[(phenoxyacetyl)amino]-, monopotassium salt, (6R,7R)- (9CI) (CA INDEX NAME)

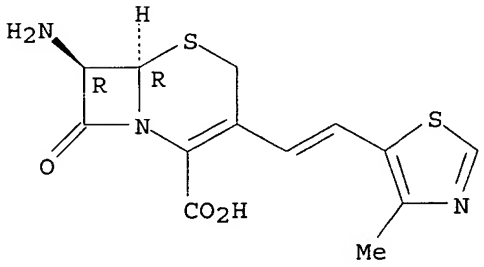
Absolute stereochemistry.
Double bond geometry unknown.



● K

IT **156925-15-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for production and purification of
7-amino-3-[(Z)-2-(4-methylthiazol-5-
yl)vinyl]-3-cephem-4-carboxylic acid)
RN 156925-15-4 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,
7-amino-3-[2-(4-methyl-5-thiazolyl)ethenyl]-8-oxo-, (6R,7R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



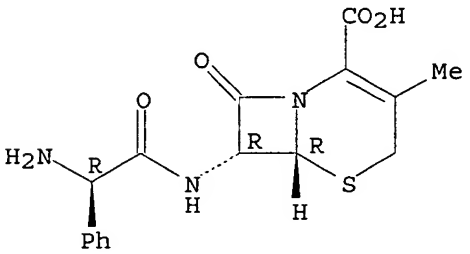
IT **9014-06-6**, Penicillin G acylase
RL: CAT (Catalyst use); USES (Uses)
(process for production and purification of
7-amino-3-[(Z)-2-(4-methylthiazol-5-
yl)vinyl]-3-cephem-4-carboxylic acid or alkali metal salts thereof by
using porous **polymers**)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:110142 CAPLUS
DOCUMENT NUMBER: 140:405508
TITLE: Evaluation of magnetic **polymer** micro-beads
as carriers of immobilised biocatalysts for selective

and stereoselective transformations
AUTHOR(S): Bozhinova, D.; Galunsky, B.; Yueping, G.; Franzreb, M.; Koester, R.; Kasche, V.
CORPORATE SOURCE: Bereich Wasser- und Geotechnologie, Forschungszentrum Karlsruhe-in der Helmholtz Gemeinschaft, Institut fuer Technische Chemie, Eggenstein-Leopoldshafen, 76344, Germany
SOURCE: Biotechnology Letters (2004), 26(4), 343-350
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 11 Feb 2004
AB The kinetic, selective and stereoselective properties of enzyme immobilized on magnetic polymer beads with diams. in the range 1 μm was studied with penicillin amidase from E. coli. The enzyme was immobilized on epoxy and glutaraldehyde-activated poly(vinyl alc.), poly(methylmetacrylate) and poly(vinyl acetate-divinylbenzene) magnetic beads. The amount of covalently bound active protein was dependent on the chemical modification of the matrix and increased at higher ionic strength of the immobilization buffer. The small size of the magnetic beads, that reduces mass transfer limitations, and the decreased charge d. in the elec. double layer resulted in lower apparent Km values and higher efficiency for benzylpenicillin hydrolysis, higher stereoselectivity in condensation of R-phenylglycine amide with S- and R-Phe and in hydrolysis of racemic phenylacetyl-Phe and higher selectivity in kinetically controlled synthesis of cephalexin compared to the enzyme immobilized on larger and porous carriers.
IT **15686-71-2P**, Cephalexin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(evaluation of magnetic **polymer** micro-beads as carriers of immobilized biocatalysts for selective and stereoselective transformations)
RN 15686-71-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9014-06-6**, Penicillin amidase
RL: BCP (Biochemical process); **CAT (Catalyst use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(magnetic **polymer** micro-beads as carriers of immobilized biocatalysts for selective and stereoselective transformations)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

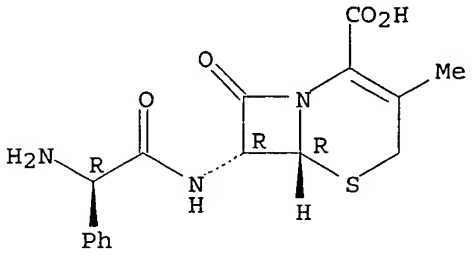
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:406886 CAPLUS
DOCUMENT NUMBER: 139:99885
TITLE: Conjugation of penicillin acylase with the reactive copolymer of N-**isopropylacrylamide**: a step toward a thermosensitive industrial biocatalyst
AUTHOR(S): Ivanov, Alexander E.; Edink, Ewald; Kumar, Ashok; Galaev, Igor Yu.; Arendsen, Alexander F.; Bruggink, Alle; Mattiasson, Bo
CORPORATE SOURCE: Department of Biotechnology Center for Chemistry and Chemical Engineering, Lund University, Lund, S-221 00, Swed.
SOURCE: Biotechnology Progress (2003), 19(4), 1167-1175
CODEN: BIPRET; ISSN: 8756-7938
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 29 May 2003
AB Conjugation of penicillin acylase (PA) to poly-N-**isopropylacrylamide** (polyNIPAM) was studied as a way to prepare a thermosensitive biocatalyst for industrial applications to antibiotic synthesis. Condensation of PA with the copolymer of NIPAM containing active ester groups resulted in higher coupling yields of the enzyme (37%) compared to its chemical modification and copolymn. with the monomer (9% coupling yield) at the same NIPAM:enzyme weight ratio of ca. 35. A 10-fold increase of the enzyme loading on the copolymer resulted in 24% coupling yield and increased by 4-fold the specific PA activity of the conjugate. Two mol. forms of the conjugate were found by gel filtration on Sepharose CL 4B: the lower mol. weight fraction of ca. 106 and, presumably, cross-linked protein-polymer aggregates of MW > 107. Michaelis constant for 5-nitro-3-phenylacetamidobenzoic acid hydrolysis by the PA conjugate (20 μM) was found to be slightly higher than that of the free enzyme (12 μM), and evaluation of Vmax testifies to the high catalytic efficiency of the conjugated enzyme. PolyNIPAM-cross-linked PA retained its capacity to synthesize cephalexin from D-phenylglycinamide and 7-aminodeacetoxycephalosporanic acid. The synthesis-hydrolysis ratios of free and polyNIPAM-cross-linked enzyme in cephalexin synthesis were 7.46 and 7.49, resp. Thus, diffusional limitation, which is a problem in the industrial production of β-lactam antibiotics, can be successfully eliminated by crosslinking penicillin acylase to a smart polymer (i.e., polyNIPAM).
IT **9014-06-6DP**, Penicillin Acylase, conjugated to N-**isopropylacrylamide polymers** and copolymers
RL: BCP (Biochemical process); **CAT (Catalyst use)**; PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(conjugation of penicillin acylase with N-**isopropylacrylamide** copolymers for cephalexin biosynthesis)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **15686-71-2P**, Cephalexin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(conjugation of penicillin acylase with N-**isopropylacrylamide**

copolymers for cephalexin biosynthesis)
RN 15686-71-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9014-06-6**, Penicillin Acylase
RL: RCT (Reactant); RACT (Reactant or reagent)
(conjugation of penicillin acylase with N-**isopropylacrylamide** copolymers for cephalexin biosynthesis)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

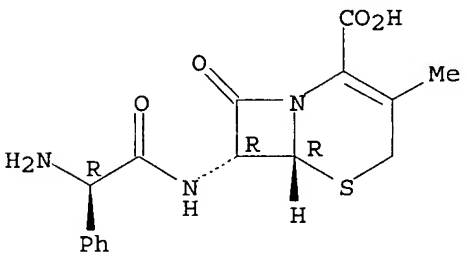
L37 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:562268 CAPLUS
DOCUMENT NUMBER: 137:261927
TITLE: Enzyme Reaction Engineering: Effect of Methanol on the Synthesis of Antibiotics Catalyzed by Immobilized Penicillin G Acylase under Isothermal and Non-Isothermal Conditions
AUTHOR(S): Travascio, P.; Zito, E.; Portaccio, M.; Diano, N.; Grano, V.; Di Martino, S.; Bertolini, T.; Rossi, S.; Mita, D. G.
CORPORATE SOURCE: International Institute of Genetics and Biophysics of CNR, Naples, 80125, Italy
SOURCE: Biotechnology Progress (2002), 18(5), 975-985
CODEN: BIPRET; ISSN: 8756-7938
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:261927
ED Entered STN: 30 Jul 2002
AB The effect of methanol on the kinetically controlled synthesis of cephalexin by free and immobilized penicillin G acylase (PGA) was investigated. Catalytic and hydrophobic membranes were obtained by chemical grafting, activation, and PGA immobilization on hydrophobic nylon supports. Bu **methacrylate** (BMA) was used as graft monomer. Increasing concns. of methanol were found to cause a greater deleterious effect on the activity of free than on that of the immobilized enzyme. Methanol, however, improved the kinetic stability of cephalexin synthesized by free PGA, resulting in higher maximum yields. By contrast, immobilized PGA reached 100% yields even in the absence of the cosolvent. Cephalexin synthesis by the catalytic membrane was also performed in a

non-isothermal bioreactor. Under these conditions, a 94% increase of the synthetic activity and complete conversion of the limiting substrate to cephalexin were obtained. The addition of methanol reduced the non-isothermal activity increase. The phys. cause responsible for the non-isothermal behavior of the hydrophobic catalytic membrane was identified in the process of thermodialysis.

IT **9014-06-6DP**, immobilized on nylon **butylmethacrylate** graft copolymer
RL: BCP (Biochemical process); **CAT (Catalyst use)**; SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(effect of methanol on enzymic synthesis of cephalexin with membrane immobilized penicillin G acylase)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **15686-71-2P**, Cephalexin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(effect of methanol on enzymic synthesis of cephalexin with membrane immobilized penicillin G acylase)
RN 15686-71-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9014-06-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(effect of methanol on enzymic synthesis of cephalexin with membrane immobilized penicillin G acylase)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:554688 CAPLUS
DOCUMENT NUMBER: 137:246582
TITLE: Advantages of using non-isothermal bioreactors for the enzymatic synthesis of antibiotics: the Penicillin G acylase as enzyme model
AUTHOR(S): Travascio, P.; Zito, E.; De Maio, A.; Schroen, C. G. P. H.; Durante, D.; De Luca, P.; Bencivenga, U.; Mita, D. G.

Searched by Barb O'Bryen, STIC 2-2518

CORPORATE SOURCE: International Institute of Genetics and Biophysics of CNR, Naples, 80125, Italy
SOURCE: Biotechnology and Bioengineering (2002), 79(3), 334-346
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 26 Jul 2002

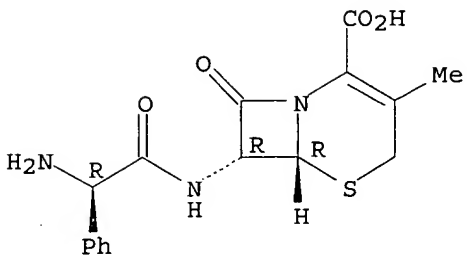
AB A new hydrophobic and catalytic membrane was prepared by immobilizing Penicillin G acylase (PGA, EC.3.5.1.11) from E. coli on a nylon membrane, chemical grafted with **butylmethacrylate** (BMA). Hexamethylenediamine (HMDA) and glutaraldehyde (Glu) were used as a spacer and coupling agent, resp. PGA was used for the enzymic synthesis of cephalexin, using D(-)-phenylglycine Me ester (PGME) and 7-amino-3-deacetoxycephalosporanic acid (7-ADCA) as substrates. Several factors affecting this reaction, such as pH, temperature, and concns. of substrates were investigated. The results indicated good enzyme-binding efficiency of the pre-treated membrane, and an increased stability of the immobilized PGA towards pH and temperature Calcn. of the activation energies showed that cephalexin production by the immobilized biocatalyst was limited by diffusion, resulting in a decrease of enzyme activity and substrate affinity. Temperature gradients were employed as a way to reduce the effects of diffusion limitation. Cephalexin was found to linearly increase with the applied temperature gradient. A temperature difference of about 3°C across the catalytic membrane resulted into a cephalexin synthesis increase of 100% with a 50% reduction of the production times. The advantage of using non-isothermal bioreactors in biotechnol. processes, including pharmaceutical applications, is also discussed.

IT **9014-06-6DP**, immobilized on nylon **butylmethacrylate** graft copolymer
RL: BCP (Biochemical process); **CAT (Catalyst use)**; SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(enzymic synthesis of cephalexin with membrane immobilized penicillin G acylase in a non-isothermal bioreactor)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **15686-71-2P**, Cephalexin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(enzymic synthesis of cephalexin with membrane immobilized penicillin G acylase in a non-isothermal bioreactor)
RN 15686-71-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9014-06-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(enzymic synthesis of cephalexin with membrane immobilized penicillin G acylase in a non-isothermal bioreactor)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:497986 CAPLUS
DOCUMENT NUMBER: 138:121650
TITLE: Kinetic and thermodynamic approach to design of processes for enzymatic synthesis of beta lactams
AUTHOR(S): Kurochkina, V. B.; Nys, P. S.
CORPORATE SOURCE: National Research Centre for Antibiotics, Moscow, 113105, Russia
SOURCE: Biocatalysis and Biotransformation (2002), 20(1), 35-41
CODEN: BOBOEQ; ISSN: 1024-2422
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 02 Jul 2002
AB An optimal way to design an enzymic process for the production of beta lactam antibiotics based on thermodn. and kinetic studies is described. The study was performed on model reactions involving synthesis of cephalosporin-acids (cephalothin, cefazolin, cefoxitin) using immobilized cephalosporin-acid synthetase from Escherichia coli as biocatalyst, and aminocephalosporins (cephalexin) using immobilized cells of Xanthomonas rubrilineans containing the aminocephalosporin synthetase. The possibility of direct synthesis of cephalothin and cefoxitin was shown, the main equilibrium parameters were determined and the operation conditions were evaluated. The maximum key amino acid conversion to product of approx. 90% for cefoxitin and cephalothin was achieved using initial concns. of the corresponding key amino acids of 0.05 M and, resp., 2-fold and 4-fold molar excess of the carboxylic acids. Cefazolin and cephalexin production by enzymic synthesis with using of corresponding biocatalyst with a mechanism of action involving the acylenzyme intermediate was shown possible. The kinetic parameters of the process were estimated and the relationship between the maximum antibiotic yield and the initial concns. of the substrate and nucleophile in the kinetically controlled synthesis was determined The technologies for cefazolin and cephalexin enzymic synthesis were designed and the cefazolin technol. was optimized. Maximum yields of cefazolin and cephalexin of more than 90% were predicted by the kinetic model using 4-6-fold molar

excess of the acylating agents and maximum yields of approx. 85% were achieved in expts.

IT **9014-06-6D**, Penicillin amidase, covalently immobilized in **polyacrylamide**
RL: BCP (Biochemical process); **CAT (Catalyst use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(kinetic and thermodn. approach to design of processes for enzymic synthesis of beta lactams)

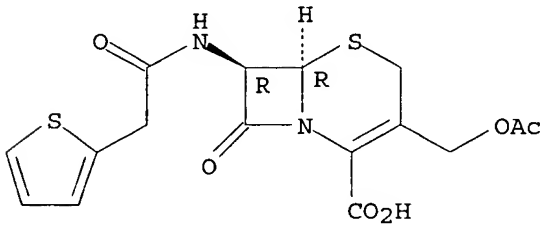
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **153-61-7P**, Cephalothin **15686-71-2P**, Cephalexin **25953-19-9P**, Cefazolin **35607-66-0P**, Cefoxitin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(kinetic and thermodn. approach to design of processes for enzymic synthesis of beta lactams)

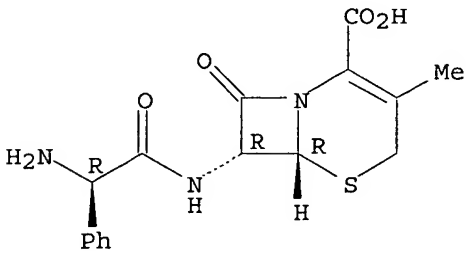
RN 153-61-7 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[(acetyloxy)methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



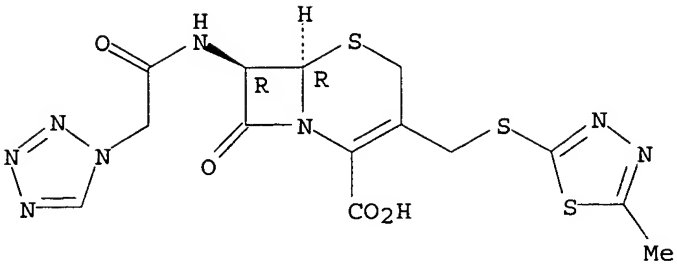
RN 15686-71-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



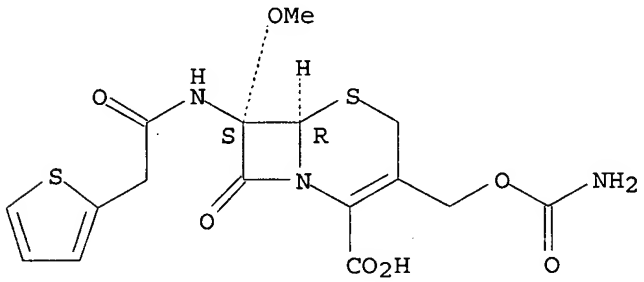
RN 25953-19-9 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[(5-methyl-1,3,4-thiadiazol-2-yl)thio]methyl]-8-oxo-7-[(1H-tetrazol-1-ylacetyl)amino]-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 35607-66-0 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[(aminocarbonyl)oxy]methyl]-7-methoxy-8-oxo-7-[(2-thienylacetyl)amino]-, (6R,7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:187184 CAPLUS
DOCUMENT NUMBER: 126:183181
TITLE: Immobilized penicillin G acylase for improved synthesis of β-lactam antibiotics
INVENTOR(S): De Vroom, Erik
PATENT ASSIGNEE(S): Gist-Brocades B.V., Neth.; De Vroom, Erik
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9704086	A1	19970206	WO 1996-EP3253	19960716
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9666592	A1	19970218	AU 1996-66592	19960716
CN 1190990	A	19980819	CN 1996-195543	19960716
JP 2001527381	T2	20011225	JP 1997-506326	19960716

CN 1572873	A	20050202	CN 2004-10063362	19960716
EP 839192	A1	19980506	EP 1996-926389	19970716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
US 6060268	A	20000509	US 1998-983370	19980115
PRIORITY APPLN. INFO.:			EP 1995-201979	A 19950718
			US 1995-1477P	P 19950718
			CN 1996-195543	A3 19960716
			WO 1996-EP3253	W 19960716

ED Entered STN: 21 Mar 1997

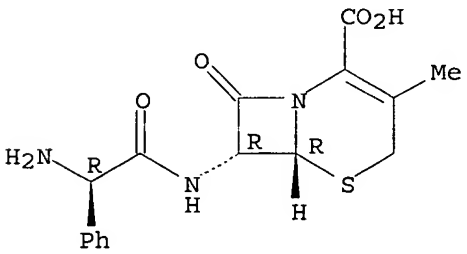
AB A new immobilized penicillin G acylase with a surprisingly good performance is provided by using a carrier consisting of a gelling agent (e.g., gelatin) and a polymer containing free amino groups (e.g., alginate amine, chitosan, pectin, or polyethylene imine). By applying this new immobilized enzyme, β-lactam derivs. are prepared in high yield by enzymic reaction of a parent amino β-lactam and a corresponding acylating agent. Thus, amoxycillin is synthesized by adding 50 U of immobilized Escherichia coli penicillin G acylase to 50 mL of 10 mM D-4-hydroxyphenylglycine amide and 30 mM 6-amino-penicillanic acid at 21°. The pH is adjusted to 5.0 and the reaction is allowed to proceed under a nitrogen atmospheric with pH control using a 0.05M solution of H_2SO_4 in water. The molar ratio synthesis/hydrolysis in the condensation reaction is superior to that of penicillin G acylases immobilized on other carriers.

IT **15686-71-2P**, Cephalexin **38821-53-3P**, Cephradine
50370-12-2P, Cephadroxil **53994-73-3P**, Cephaclor
92665-29-7P, Cefprozil
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(improved immobilized penicillin G acylase for synthesis of β-lactam antibiotics)

RN 15686-71-2 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

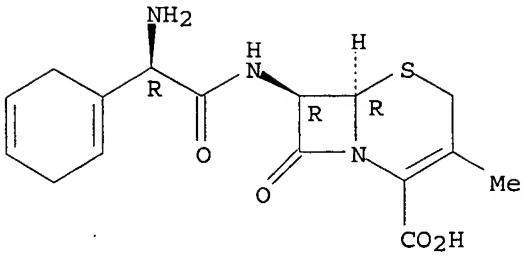
Absolute stereochemistry.



RN 38821-53-3 CAPLUS

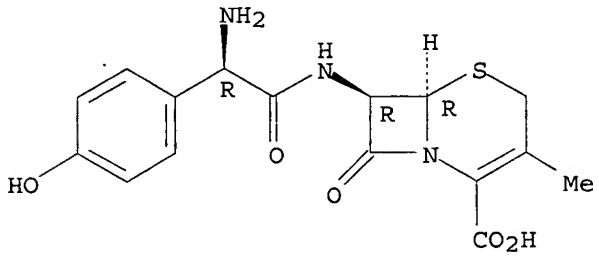
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-amino-1,4-cyclohexadien-1-ylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



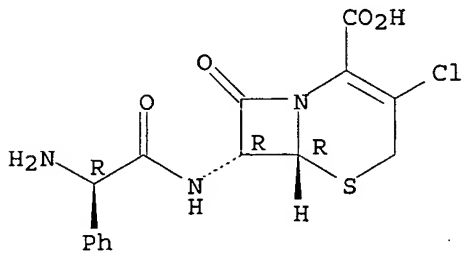
RN 50370-12-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-amino(4-hydroxyphenyl)acetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



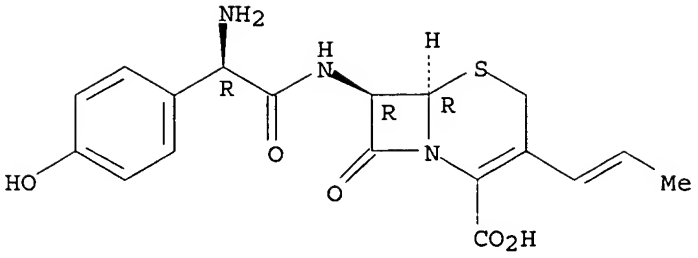
RN 53994-73-3 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-chloro-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 92665-29-7 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-amino(4-hydroxyphenyl)acetyl]amino]-8-oxo-3-(1-propenyl)-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

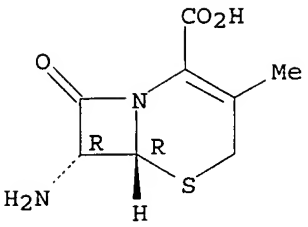


IT **9014-06-6**
RL: CAT (Catalyst use); USES (Uses)
(improved immobilized penicillin G acylase for synthesis of β-lactam antibiotics)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L37 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:683051 CAPLUS
DOCUMENT NUMBER: 127:356524
TITLE: Hydrolysis of cephalosporin G to 7-amino-3-deacetoxycefalosporanic acid by immobilized penicillin acylase
AUTHOR(S): Xu, Guanzhu; Han, Hui; Wang, Zhenxiang; Gao, Hongqing; Zhao, Li
CORPORATE SOURCE: Institute of Microbiology, Academia Sinica, Beijing, 100080, Peop. Rep. China
SOURCE: Weishengwu Xuebao (1997), 37(3), 190-195
CODEN: WSHPA8; ISSN: 0001-6209
PUBLISHER: Kexue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
ED Entered STN: 29 Oct 1997
AB The extracellular penicillin G acylase (PA) of Bacillus megaterium was immobilized on polyacrylonitrile fibers by coupling. The optimal pH and temperature values of the immobilized penicillin acylase (IMPA) for the hydrolysis of cephalosporin G(cep G) were 9.0 and 50° resp. The apparent Michaelis constant for Cep G was 1.67+10-2 mol/L and the Vm was 3.01 mmol g-1 min-1 at 37°, pH 8.0. 5-6% Cephalosporin G and 300 U activity of the IMPA for 1 g cephalosporin G were used. The remained activity was 77.8% after operating 25 times and the yield of 7-ADCA was 92.68%.
IT **22252-43-3P**, 7-Adca
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(hydrolysis of cephalosporin G to 7-amino-3-deacetoxycefalosporanic acid by immobilized penicillin acylase)
RN 22252-43-3 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

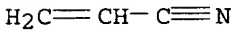
Absolute stereochemistry.



IT **25014-41-9**, Polyacrylonitrile
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hydrolysis of cephalosporin G to 7-amino-3-deacetoxycefalosporanic acid by immobilized penicillin acylase)
RN 25014-41-9 CAPLUS
CN 2-Propenenitrile, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 107-13-1
CMF C3 H3 N



IT **9014-06-6**
RL: **CAT (Catalyst use)**; PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(hydrolysis of cephalosporin G to 7-amino-3-deacetoxycefalosporanic acid by immobilized penicillin acylase)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L37 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:240224 CAPLUS
DOCUMENT NUMBER: 124:287199
TITLE: Membrane filtration process for 6-aminopenicillanic acid
INVENTOR(S): Lopez, Jorge L.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

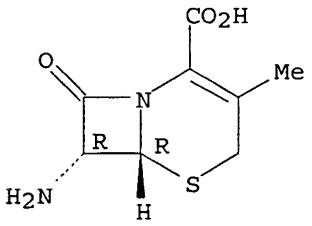
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5500352	A	19960319	US 1993-36327	19930324
US 5521068	A	19960528	US 1995-385859	19950209

PRIORITY APPLN. INFO.: US 1993-36327 A3 19930324
ED Entered STN: 24 Apr 1996
AB The invention relates to an improved process for converting 6-acylaminopenicillanic acid to 6-aminopenicillanic acid (6-APA). The

process employs a solution or suspension of penicillin acylase from which the product is separated after reaction by ultrafiltration through a particular class of polymer membranes. The process may also be applied to the production of 7-aminodesacetoxycephalosporanic acid and can be incorporated into an improved, streamlined process for obtaining 6-APA from fermentation broths.

IT **22252-43-3P**, 7-Aminodesacetoxycephalosporanic acid
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(6-aminopenicillanic acid production using penicillin acylase with membrane filtration process)
RN 22252-43-3 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

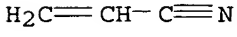


IT **9014-06-6**, Penicillin acylase
RL: **CAT (Catalyst use)**; USES (Uses)
(6-aminopenicillanic acid production using penicillin acylase with membrane filtration process)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **25014-41-9**, Polyacrylonitrile
RL: NUU (Other use, unclassified); USES (Uses)
(6-aminopenicillanic acid production using penicillin acylase with polyacrylonitrile membrane filtration process)
RN 25014-41-9 CAPLUS
CN 2-Propenenitrile, homopolymer (9CI) (CA INDEX NAME)

CM 1

CRN 107-13-1
CMF C3 H3 N



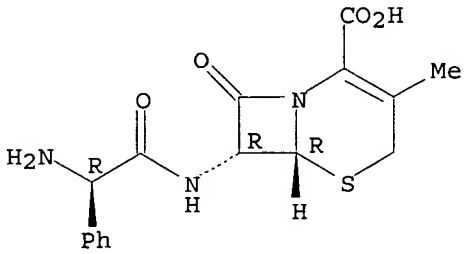
L37 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:596175 CAPLUS
DOCUMENT NUMBER: 125:219754
TITLE: Improved enzymic process for producing penicillins and cephalosporins
INVENTOR(S): Zenoni, Maurizio
PATENT ASSIGNEE(S): Acs Dobfar S.P.A., Italy
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 730035	A1	19960904	EP 1995-120490	19951222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2167118	AA	19960829	CA 1996-2167118	19960112
ZA 9601015	A	19960820	ZA 1996-1015	19960208
ZA 9601014	A	19960829	ZA 1996-1014	19960208
JP 08242884	A2	19960924	JP 1996-30699	19960219
CN 1144274	A	19970305	CN 1996-102535	19960226
BR 9600830	A	19971230	BR 1996-830	19960227
AU 9645798	A1	19960905	AU 1996-45798	19960228
PRIORITY APPLN. INFO.:			IT 1995-MI383 A	19950228

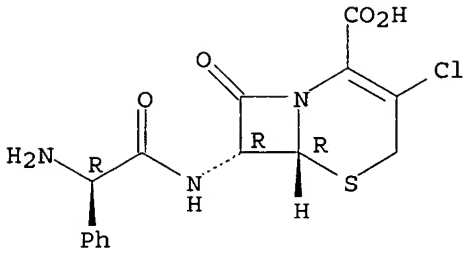
OTHER SOURCE(S): CASREACT 125:219754; MARPAT 125:219754
ED Entered STN: 07 Oct 1996
AB A process for producing penicillins or cephalosporins by reacting a 6-aminopenicillanic acid or a 7-aminocephalosporanic acid in aqueous medium with an amide in the presence of immobilized penicillin acylase is claimed.
IT **15686-71-2P**, Cephalexin **53994-73-3P**, Cefaclor
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(producing penicillins and cephalosporins using immobilized penicillin acylase)
RN 15686-71-2 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-methyl-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 53994-73-3 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2R)-aminophenylacetyl]amino]-3-chloro-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

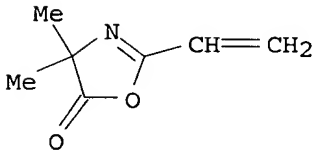


IT **9014-06-6**, Penicillin acylase
RL: **CAT (Catalyst use)**; USES (Uses)
(producing penicillins and cephalosporins using immobilized penicillin acylase)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **129825-50-9**
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(producing penicillins and cephalosporins using penicillin acylase immobilized on)
RN 129825-50-9 CAPLUS
CN 2-Propenamide, N,N'-methylenebis-, polymer with 2-ethenyl-4,4-dimethyl-5(4H)-oxazolone (9CI) (CA INDEX NAME)

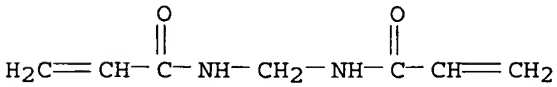
CM 1

CRN 29513-26-6
CMF C7 H9 N O2



CM 2

CRN 110-26-9
CMF C7 H10 N2 O2



L37 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:76123 CAPLUS
DOCUMENT NUMBER: 118:76123
TITLE: Solid granular immobilized G-penicillinamidase for

6-aminopenicillanic acid and 7-aminodeacetoxycephalosporanoic acid production from benzylpenicillin and deacetoxycephalosporin G

INVENTOR(S): Becka, Stanislav; Vojtisek, Vladimir; Hasal, Pavel; Krumphanzl, Vladimir; Slavicek, Frantisek

PATENT ASSIGNEE(S): Mikrobiologicky Ustav, Czech.

SOURCE: Czech., 6 pp.
CODEN: CZXXA9

DOCUMENT TYPE: Patent

LANGUAGE: Czech

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 274906	B2	19911217	CS 1989-3621	19890615

PRIORITY APPLN. INFO.: CS 1989-3621 19890615

ED Entered STN: 02 Mar 1993

AB A method for the preparation of granular biocatalyst with immobilized G-penicillinamidase is described. The enzyme isolated and purified from bacterial sources is mixed with water-soluble reactive polymers prepared from polyethyleneimine, diamines, diamino acids, glutaraldehyde, and other components. The formed particles are separated, sieved, dried, washed with water, and standardized.

IT **9014-06-6**
RL: PROC (Process)
(immobilization of, in granular **polymer**)

RN 9014-06-6 CAPLUS

CN Amidase, penicillin (9CI) (CA INDEX NAME)

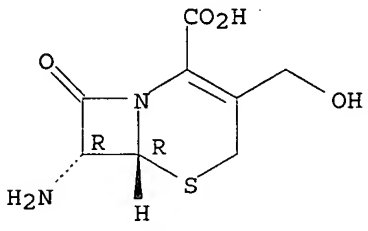
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **15690-38-7P**
RL: PREP (Preparation)
(preparation of, by benzylpenicillin hydrolysis by penicillinamidase immobilized in granular **polymer**)

RN 15690-38-7 CAPLUS

CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-(hydroxymethyl)-8-oxo-, (6R,7R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L37 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1977:137941 CAPLUS

DOCUMENT NUMBER: 86:137941

TITLE: Purification of products resulting from the enzymic splitting of β-lactam antibiotic

INVENTOR(S): Hueper, Fritz; Oberheiden, Helmut

PATENT ASSIGNEE(S): Bayer A.-G., Fed. Rep. Ger.

SOURCE: Ger. Offen., 20 pp.

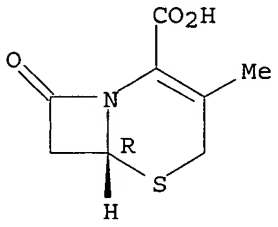
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2528622	A1	19770113	DE 1975-2528622	19750626
US 4113941	A	19780912	US 1976-692876	19760604
NL 7606855	A	19761228	NL 1976-6855	19760623
GB 1531329	A	19781108	GB 1976-26286	19760624

PRIORITY APPLN. INFO.: DE 1975-2528622 A 19750626
ED Entered STN: 12 May 1984
AB β-Lactam antibiotics were cleaved enzymically and the reaction products purified on a column of quaternary ammonium ion-exchange resin. Thus, 65.5 g K penicillin G [113-98-4] in 1 L H2O was treated with 1200 units of immobilized penicillin acylase **[9014-06-6]** and cleaved to 6-aminopenicillanic acid (I) [551-16-6] and phenylacetic acid. After separation of the enzyme preparation, the reaction mixture was pressed through a 2 cm diameter column containing 30 mL Lewatit MP 500 A [37199-41-0]. The passed solution was concentrated under vacuum (25 Torr) to 200 mL and adjusted to pH 4.2 by addition of 15% HCl in 150 mL methylisobutyl ketone and the resulting precipitate was collected and washed successively with water and acetone. The yield of I was >90%, and 2 g of the substance in 20 mL of 2N HCl had an extinction coefficient of <0.1 at 425 nm with a path length of 1 cm vs. 0.31 for the brown colored powder obtained similarly but without the Lewatit treatment step.
IT **9014-06-6**
RL: PROC (Process)
(immobilization of)
RN 9014-06-6 CAPLUS
CN Amidase, penicillin (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **51088-26-7P**
RL: PUR (Purification or recovery); PREP (Preparation)
(purification of, on anion exchange **resins**)
RN 51088-26-7 CAPLUS
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-methyl-8-oxo-, (6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



FILE 'HOME' ENTERED AT 15:01:21 ON 19 OCT 2006

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=> d stat que l6; d his nofile
L4              STR
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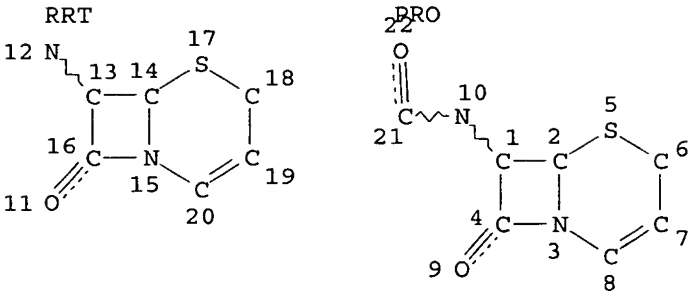

Search history

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  22

STEREO ATTRIBUTES: NONE
L6          909 SEA FILE=CASREACT SSS FUL L4 ( 11379 REACTIONS)

100.0% DONE   11500 VERIFIED   11379 HIT RXNS                  909 DOCS
SEARCH TIME: 00.00.02



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     FILE 'REGISTRY' ENTERED AT 14:48:53 ON 19 OCT 2006
L1            51 SEA ABB=ON  PENICILLIN AMIDASE?/CN

     FILE 'CASREACT' ENTERED AT 14:49:11 ON 19 OCT 2006
L2                STR
L3             50 SEA SSS SAM L2 (   679 REACTIONS)
L4                STR L2
L5             50 SEA SSS SAM L4 (   662 REACTIONS)
L6            909 SEA SSS FUL L4 ( 11379 REACTIONS)
                  SAVE TEMP L6 BER140CASRE1/A
L7            122 SEA ABB=ON  L1/CAT
L8             35 SEA ABB=ON  L6 AND L7
L9          26925 SEA ABB=ON  POLYMER? OR RESIN#
L10             3 SEA ABB=ON  L8 AND L9
L11          4600 SEA ABB=ON  COAT? OR IMMOBILI?
L12            19 SEA ABB=ON  L8 AND (L9 OR L11)

     FILE 'CAPLUS' ENTERED AT 14:55:44 ON 19 OCT 2006
                  D SAVED
                  ACT BER140CAAU/A
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L13             1 SEA ABB=ON  US2004-501140/AP
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                  ACT BER140CA1/A
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L14 (      84829)SEA ABB=ON  191.74.3/RID
L15 (       7691)SEA ABB=ON  L14/P
L16 (         51)SEA ABB=ON  PENICILLIN AMIDASE?/CN
L17 (       1995)SEA ABB=ON  L16
L18 (    1525213)SEA ABB=ON  POLYMER?/OBI
L19 (     484949)SEA ABB=ON  RESIN#/OBI
L20           10 SEA ABB=ON  L15 AND L17 AND (L18 OR L19)
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                ACT BER140CA2/A
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L21 (      84829)SEA ABB=ON  191.74.3/RID
L22 (       7691)SEA ABB=ON  L21/P
L23 (         51)SEA ABB=ON  PENICILLIN AMIDASE?/CN
L24 (       1995)SEA ABB=ON  L23
L25 (        363)SEA ABB=ON  L24(L)CAT/RL
L26 (     416467)SEA ABB=ON  ?ACRYLAMID?/BI OR ?METHACRYL?/BI
L27 (          1)SEA ABB=ON  25014-41-9
L28 (          1)SEA ABB=ON  129825-50-9
L29 (      16503)SEA ABB=ON  (L27 OR L28)
L30           11 SEA ABB=ON  L25 AND L22 AND (L26 OR L29)
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                E MENZLER/AU
L31            1 SEA ABB=ON  MENZLER S?/AU
L32           40 SEA ABB=ON  MEIER C?/AU
L33            4 SEA ABB=ON  BOLLER T?/AU
L34            0 SEA ABB=ON  PETEREIT H?/AU
L35            0 SEA ABB=ON  (L31 OR L33) AND L32
                D SCAN TI L31

     FILE 'CAPLUS' ENTERED AT 14:59:04 ON 19 OCT 2006
                D QUE L13
                D IBIB ED ABS L13

     FILE 'CAPLUS' ENTERED AT 14:59:35 ON 19 OCT 2006
                D QUE L20
                D QUE L30
L36           15 SEA ABB=ON  (L20 OR L30) NOT L13

     FILE 'CASREACT' ENTERED AT 14:59:52 ON 19 OCT 2006
                D STAT QUE L6
                D QUE NOS L12

     FILE 'CASREACT, CAPLUS' ENTERED AT 14:59:57 ON 19 OCT 2006
L37           33 DUP REM L12 L36 (1 DUPLICATE REMOVED)
                     ANSWERS '1-19' FROM FILE CASREACT
                     ANSWERS '20-33' FROM FILE CAPLUS
                D IBIB ABS HIT 1-19
                D IBIB ED ABS HITSTR 20-33

     FILE 'HOME' ENTERED AT 15:01:21 ON 19 OCT 2006
                D STAT QUE L6

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